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- (71) Applicant: **MANNKIND CORPORATION** [US/US];
28903 North Avenue Paine, Valencia, CA 91355 (US).
- (72) Inventors: **SIMARD, John, J.,L.**; Suite #7, 1684 Alberni
Street, Vancouver, British Columbia Z6G1A6 (CA). **DIA-**
MOND, David, C.; 23135 Schoenborn Street, West Hills,
CA 91304 (US). **LIU, Liping**; 22228 Victory Boulevard,
H-111, Woodland Hills, CA 91367 (US). **LIU, Zheng**;
22216 Victory Boulevard, C302, Woodland Hills, CA
91367 (US).
- (74) Agent: **MALLON, Joseph, J.**; KNOBBE, MARTENS,
OLSON & BEAR, LLP, 2040 Main Street, 14th Floor,
Irvine, CA 92614 (US).

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ning of each regular issue of the PCT Gazette.*

(54) Title: EPITOPE SEQUENCES

(57) Abstract: Disclosed herein are polypeptides, including epitopes, clusters, and antigens. Also disclosed are compositions that include said polypeptides and methods for their use.



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EPITOPE SEQUENCES

Background of the Invention

Field of the Invention

5 The present invention generally relates to peptides, and nucleic acids encoding peptides, that are useful epitopes of target-associated antigens. More specifically, the invention relates to epitopes that have a high affinity for MHC class I and that are produced by target-specific proteasomes.

Description of the Related Art

10 Neoplasia and the Immune System

 The neoplastic disease state commonly known as cancer is thought to result generally from a single cell growing out of control. The uncontrolled growth state typically results from a multi-step process in which a series of cellular systems fail, resulting in the genesis of a neoplastic cell. The resulting neoplastic cell rapidly reproduces itself, forms one or more tumors, and eventually
15 may cause the death of the host.

 Because the progenitor of the neoplastic cell shares the host's genetic material, neoplastic cells are largely unassailed by the host's immune system. During immune surveillance, the process in which the host's immune system surveys and localizes foreign materials, a neoplastic cell will appear to the host's immune surveillance machinery as a "self" cell.

20 Viruses and the Immune System

 In contrast to cancer cells, virus infection involves the expression of clearly non-self antigens. As a result, many virus infections are successfully dealt with by the immune system with minimal clinical sequela. Moreover, it has been possible to develop effective vaccines for many of those infections that do cause serious disease. A variety of vaccine approaches have been used
25 successfully to combat various diseases. These approaches include subunit vaccines consisting of individual proteins produced through recombinant DNA technology. Notwithstanding these advances, the selection and effective administration of minimal epitopes for use as viral vaccines has remained problematic.

 In addition to the difficulties involved in epitope selection stands the problem of viruses
30 that have evolved the capability of evading a host's immune system. Many viruses, especially viruses that establish persistent infections, such as members of the herpes and pox virus families, produce immunomodulatory molecules that permit the virus to evade the host's immune system. The effects of these immunomodulatory molecules on antigen presentation may be overcome by the targeting of select epitopes for administration as immunogenic compositions. To better
35 understand the interaction of neoplastic cells and virally infected cells with the host's immune system, a discussion of the system's components follows below.

The immune system functions to discriminate molecules endogenous to an organism ("self" molecules) from material exogenous or foreign to the organism ("non-self" molecules). The immune system has two types of adaptive responses to foreign bodies based on the components that mediate the response: a humoral response and a cell-mediated response. The humoral response is mediated by antibodies, while the cell-mediated response involves cells classified as lymphocytes. Recent anticancer and antiviral strategies have focused on mobilizing the host immune system as a means of anticancer or antiviral treatment or therapy.

The immune system functions in three phases to protect the host from foreign bodies: the cognitive phase, the activation phase, and the effector phase. In the cognitive phase, the immune system recognizes and signals the presence of a foreign antigen or invader in the body. The foreign antigen can be, for example, a cell surface marker from a neoplastic cell or a viral protein. Once the system is aware of an invading body, antigen specific cells of the immune system proliferate and differentiate in response to the invader-triggered signals. The last stage is the effector stage in which the effector cells of the immune system respond to and neutralize the detected invader.

An array of effector cells implements an immune response to an invader. One type of effector cell, the B cell, generates antibodies targeted against foreign antigens encountered by the host. In combination with the complement system, antibodies direct the destruction of cells or organisms bearing the targeted antigen. Another type of effector cell is the natural killer cell (NK cell), a type of lymphocyte having the capacity to spontaneously recognize and destroy a variety of virus infected cells as well as malignant cell types. The method used by NK cells to recognize target cells is poorly understood.

Another type of effector cell, the T cell, has members classified into three subcategories, each playing a different role in the immune response. Helper T cells secrete cytokines which stimulate the proliferation of other cells necessary for mounting an effective immune response, while suppressor T cells down-regulate the immune response. A third category of T cell, the cytotoxic T cell (CTL), is capable of directly lysing a targeted cell presenting a foreign antigen on its surface.

The Major Histocompatibility Complex and T Cell Target Recognition

T cells are antigen-specific immune cells that function in response to specific antigen signals. B lymphocytes and the antibodies they produce are also antigen-specific entities. However, unlike B lymphocytes, T cells do not respond to antigens in a free or soluble form. For a T cell to respond to an antigen, it requires the antigen to be processed to peptides which are then bound to a presenting structure encoded in the major histocompatibility complex (MHC). This requirement is called "MHC restriction" and it is the mechanism by which T cells differentiate "self" from "non-self" cells. If an antigen is not displayed by a recognizable MHC molecule, the T cell will not recognize and act on the antigen signal. T cells specific for a peptide bound to a

recognizable MHC molecule bind to these MHC-peptide complexes and proceed to the next stages of the immune response.

There are two types of MHC, class I MHC and class II MHC. T Helper cells ($CD4^+$) predominately interact with class II MHC proteins while cytolytic T cells ($CD8^+$) predominately interact with class I MHC proteins. Both classes of MHC protein are transmembrane proteins with a majority of their structure on the external surface of the cell. Additionally, both classes of MHC proteins have a peptide binding cleft on their external portions. It is in this cleft that small fragments of proteins, endogenous or foreign, are bound and presented to the extracellular environment.

Cells called "professional antigen presenting cells" (pAPCs) display antigens to T cells using the MHC proteins but additionally express various co-stimulatory molecules depending on the particular state of differentiation/activation of the pAPC. When T cells, specific for the peptide bound to a recognizable MHC protein, bind to these MHC-peptide complexes on pAPCs, the specific co-stimulatory molecules that act upon the T cell direct the path of differentiation/activation taken by the T cell. That is, the co-stimulation molecules affect how the T cell will act on antigenic signals in future encounters as it proceeds to the next stages of the immune response.

As discussed above, neoplastic cells are largely ignored by the immune system. A great deal of effort is now being expended in an attempt to harness a host's immune system to aid in combating the presence of neoplastic cells in a host. One such area of research involves the formulation of anticancer vaccines.

Anticancer Vaccines

Among the various weapons available to an oncologist in the battle against cancer is the immune system of the patient. Work has been done in various attempts to cause the immune system to combat cancer or neoplastic diseases. Unfortunately, the results to date have been largely disappointing. One area of particular interest involves the generation and use of anticancer vaccines.

To generate a vaccine or other immunogenic composition, it is necessary to introduce to a subject an antigen or epitope against which an immune response may be mounted. Although neoplastic cells are derived from and therefore are substantially identical to normal cells on a genetic level, many neoplastic cells are known to present tumor-associated antigens (TuAAs). In theory, these antigens could be used by a subject's immune system to recognize these antigens and attack the neoplastic cells. In reality, however, neoplastic cells generally appear to be ignored by the host's immune system.

A number of different strategies have been developed in an attempt to generate vaccines with activity against neoplastic cells. These strategies include the use of tumor-associated antigens

as immunogens. For example, U.S. Patent No. 5,993,828, describes a method for producing an immune response against a particular subunit of the Urinary Tumor Associated Antigen by administering to a subject an effective dose of a composition comprising inactivated tumor cells having the Urinary Tumor Associated Antigen on the cell surface and at least one tumor associated antigen selected from the group consisting of GM-2, GD-2, Fetal Antigen and Melanoma Associated Antigen. Accordingly, this patent describes using whole, inactivated tumor cells as the immunogen in an anticancer vaccine.

Another strategy used with anticancer vaccines involves administering a composition containing isolated tumor antigens. In one approach, MAGE-A1 antigenic peptides were used as an immunogen. (See Chaux, P., *et al.*, "Identification of Five MAGE-A1 Epitopes Recognized by Cytolytic T Lymphocytes Obtained by *In Vitro* Stimulation with Dendritic Cells Transduced with MAGE-A1," J. Immunol., 163(5):2928-2936 (1999)). There have been several therapeutic trials using MAGE-A1 peptides for vaccination, although the effectiveness of the vaccination regimes was limited. The results of some of these trials are discussed in Vose, J.M., "Tumor Antigens Recognized by T Lymphocytes," 10th European Cancer Conference, Day 2, Sept. 14, 1999.

In another example of tumor associated antigens used as vaccines, Scheinberg, *et al.* treated 12 chronic myelogenous leukemia (CML) patients already receiving interferon (IFN) or hydroxyurea with 5 injections of class I-associated bcr-abl peptides with a helper peptide plus the adjuvant QS-21. Scheinberg, D.A., *et al.*, "BCR-ABL Breakpoint Derived Oncogene Fusion Peptide Vaccines Generate Specific Immune Responses in Patients with Chronic Myelogenous Leukemia (CML) [Abstract 1665], American Society of Clinical Oncology 35th Annual Meeting, Atlanta (1999). Proliferative and delayed type hypersensitivity (DTH) T cell responses indicative of T-helper activity were elicited, but no cytolytic killer T cell activity was observed within the fresh blood samples.

Additional examples of attempts to identify TuAAs for use as vaccines are seen in the recent work of Cebon, *et al.* and Scheibenbogen, *et al.* Cebon, *et al.* immunized patients with metastatic melanoma using intradermally administered MART-1₂₆₋₃₅ peptide with IL-12 in increasing doses given either subcutaneously or intravenously. Of the first 15 patients, 1 complete remission, 1 partial remission, and 1 mixed response were noted. Immune assays for T cell generation included DTH, which was seen in patients with or without IL-12. Positive CTL assays were seen in patients with evidence of clinical benefit, but not in patients without tumor regression. Cebon, *et al.*, "Phase I Studies of Immunization with Melan-A and IL-12 in HLA A2+ Positive Patients with Stage III and IV Malignant Melanoma," [Abstract 1671], American Society of Clinical Oncology 35th Annual Meeting, Atlanta (1999).

Scheibenbogen, *et al.* immunized 18 patients with 4 HLA class I restricted tyrosinase peptides, 16 with metastatic melanoma and 2 adjuvant patients. Scheibenbogen, *et al.*,

“Vaccination with Tyrosinase peptides and GM-CSF in Metastatic Melanoma: a Phase II Trial,” [Abstract 1680], American Society of Clinical Oncology 35th Annual Meeting, Atlanta (1999). Increased CTL activity was observed in 4/15 patients, 2 adjuvant patients, and 2 patients with evidence of tumor regression. As in the trial by Cebon, *et al.*, patients with progressive disease did not show boosted immunity. In spite of the various efforts expended to date to generate efficacious anticancer vaccines, no such composition has yet been developed.

Antiviral Vaccines

Vaccine strategies to protect against viral diseases have had many successes. Perhaps the most notable of these is the progress that has been made against the disease small pox, which has been driven to extinction. The success of the polio vaccine is of a similar magnitude.

Viral vaccines can be grouped into three classifications: live attenuated virus vaccines, such as vaccinia for small pox, the Sabin poliovirus vaccine, and measles mumps and rubella; whole killed or inactivated virus vaccines, such as the Salk poliovirus vaccine, hepatitis A virus vaccine and the typical influenza virus vaccines; and subunit vaccines, such as hepatitis B. Due to their lack of a complete viral genome, subunit vaccines offer a greater degree of safety than those based on whole viruses.

The paradigm of a successful subunit vaccine is the recombinant hepatitis B vaccine based on the viruses envelope protein. Despite much academic interest in pushing the reductionist subunit concept beyond single proteins to individual epitopes, the efforts have yet to bear much fruit. Viral vaccine research has also concentrated on the induction of an antibody response although cellular responses also occur. However, many of the subunit formulations are particularly poor at generating a CTL response.

Summary of the Invention

Previous methods of priming professional antigen presenting cells (pAPCs) to display target cell epitopes have relied simply on causing the pAPCs to express target-associated antigens (TAAs), or epitopes of those antigens which are thought to have a high affinity for MHC I molecules. However, the proteasomal processing of such antigens results in presentation of epitopes on the pAPC that do not correspond to the epitopes present on the target cells.

Using the knowledge that an effective cellular immune response requires that pAPCs present the same epitope that is presented by the target cells, the present invention provides epitopes that have a high affinity for MHC I, and that correspond to the processing specificity of the housekeeping proteasome, which is active in peripheral cells. These epitopes thus correspond to those presented on target cells. The use of such epitopes in compositions, such as vaccines and other immunogenic compositions (including pharmaceutical and immunotherapeutic compositions) can activate the cellular immune response to recognize the correctly processed TAA and can result in removal of target cells that present such epitopes. In some embodiments, the housekeeping

epitopes provided herein can be used in combination with immune epitopes, generating a cellular immune response that is competent to attack target cells both before and after interferon induction. In other embodiments the epitopes are useful in the diagnosis and monitoring of the target-associated disease and in the generation of immunological reagents for such purposes.

5 Embodiments of the invention relate to isolated epitopes, antigens and/or polypeptides. The isolated antigens and/or polypeptides can include the epitopes. Preferred embodiments include an epitope or antigen having the sequence as disclosed in Tables 1A or 1B. Other embodiments can include an epitope cluster comprising a polypeptide from Tables 1A or 1B. Further, 10 embodiments include a polypeptide having substantial similarity to the already mentioned epitopes, polypeptides, antigens, or clusters. Other preferred embodiments include a polypeptide having functional similarity to any of the above. Still further embodiments relate to a nucleic acid encoding the polypeptide of any of the epitopes, clusters, antigens, and polypeptides from Tables 1A or 1B and mentioned herein.

15 For purposes of the following summary and discussion of other embodiments of the invention, reference to "the epitope," "the epitopes," or "epitope from Tables 1A or 1B" may include without limitation to all of the foregoing forms of the epitope including an epitope with the sequence set forth in the Tables or elsewhere herein, a cluster comprising such an epitope or epitopes, a polypeptide having substantial or functional similarity to those epitopes or clusters, and the like.

20 The polypeptide or epitope can be immunologically active. The polypeptide comprising the epitope can be less than about 30 amino acids in length, more preferably, the polypeptide is 8 to 10 amino acids in length, for example. Substantial or functional similarity can include addition of at least one amino acid, for example, and the at least one additional amino acid can be at an N-terminus of the polypeptide. The substantial or functional similarity can include a substitution of at 25 least one amino acid.

 The epitope, cluster, or polypeptide comprising the same can have affinity to an HLA-A2 molecule. The affinity can be determined by an assay of binding, by an assay of restriction of epitope recognition, by a prediction algorithm, and the like. The epitope, cluster, or polypeptide comprising the same can have affinity to an HLA-B7, HLA-B51 molecule, and the like.

30 In preferred embodiments the polypeptide can be a housekeeping epitope. The epitope or polypeptide can correspond to an epitope displayed on a tumor cell, to an epitope displayed on a neovasculature cell, and the like. The epitope or polypeptide can be an immune epitope. The epitope, cluster and/or polypeptide can be a nucleic acid. The epitope, cluster and/or polypeptide can be encoded by a nucleic acid.

35 Other embodiments relate to compositions, including pharmaceutical or immunogenic compositions comprising the polypeptides, including an epitope from Tables 1A or 1B, a cluster, or

a polypeptide comprising the same, and a pharmaceutically acceptable adjuvant, carrier, diluent, excipient, and the like. The adjuvant can be a polynucleotide. The polynucleotide can include a dinucleotide, which can be CpG, for example. The adjuvant can be encoded by a polynucleotide. The adjuvant can be a cytokine and the cytokine can be, for example, GM-CSF.

5 The compositions can further include a professional antigen-presenting cell (pAPC). The pAPC can be a dendritic cell, for example. The composition can further include a second epitope. The second epitope can be a polypeptide, a nucleic acid, a housekeeping epitope, an immune epitope, and the like.

10 Still further embodiments relate to compositions, including pharmaceutical and immunogenic compositions that include any of the nucleic acids discussed herein, including those that encode polypeptides that comprise epitopes or antigens from Tables 1A or 1B. Such compositions can include a pharmaceutically acceptable adjuvant, carrier, diluent, excipient, and the like.

15 Other embodiments relate to recombinant constructs that include such a nucleic acid as described herein, including those that encode polypeptides that comprise epitopes or antigens from Tables 1A or 1B. The constructs can further include a plasmid, a viral vector, an artificial chromosome, and the like. The construct can further include a sequence encoding at least one feature, such as for example, a second epitope, an IRES, an ISS, an NIS, a ubiquitin, and the like.

20 Further embodiments relate to purified antibodies that specifically bind to at least one of the epitopes in Tables 1A or 1B. Other embodiments relate to purified antibodies that specifically bind to a peptide-MHC protein complex comprising an epitope disclosed in Tables 1A or 1B or any other suitable epitope. The antibody from any embodiment can be a monoclonal antibody or a polyclonal antibody.

25 Still other embodiments relate to multimeric MHC-peptide complexes that include an epitope, such as, for example, an epitope disclosed in Tables 1A or 1B. Also, contemplated are antibodies specific for the complexes.

30 Embodiments relate to isolated T cells expressing a T cell receptor specific for an MHC-peptide complex. The complex can include an epitope, such as, for example, an epitope disclosed in Tables 1A or 1B. The T cell can be produced by an *in vitro* immunization and can be isolated from an immunized animal. Embodiments relate to T cell clones, including cloned T cells, such as those discussed above. Embodiments also relate to polyclonal population of T cells. Such populations can include a T cell, as described above, for example.

35 Still further embodiments relate to compositions, including pharmaceutical and immunogenic compositions that include a T cell, such as those described above, for example, and a pharmaceutically acceptable adjuvant, carrier, diluent, excipient, and the like.

Embodiments of the invention relate to isolated protein molecules comprising the binding domain of a T cell receptor specific for an MHC-peptide complex. The complex can include an epitope as disclosed in Tables 1A or 1B. The protein can be multivalent. Other embodiments relate to isolated nucleic acids encoding such proteins. Still further embodiments relate to recombinant constructs that include such nucleic acids.

Other embodiments of the invention relate to host cells expressing a recombinant construct as described above and elsewhere herein. The host cells can include constructs encoding an epitope, a cluster or a polypeptide comprising said epitope or said cluster. The epitope or epitope cluster can be one or more of those disclosed in Tables 1A or 1B, for example, and as otherwise defined. The host cell can be a dendritic cell, macrophage, tumor cell, tumor-derived cell, a bacterium, fungus, protozoan, and the like. Embodiments also relate to compositions, including pharmaceutical and immunogenic compositions that include a host cell, such as those discussed herein, and a pharmaceutically acceptable adjuvant, carrier, diluent, excipient, and the like.

Still other embodiments relate to compositions including immunogenic compositions, such as for example, vaccines or immunotherapeutic compositions. The compositions can include at least one component, such as, for example, an epitope disclosed in Tables 1A or 1B or otherwise described herein; a cluster that includes such an epitope, an antigen or polypeptide that includes such an epitope; a composition as described above and herein; a construct as described above and herein, a T cell, a construct comprising a nucleic acid encoding a T cell receptor binding domain specific for an MHC-peptide complex and compositions including the same, a host cell as described above and herein, and compositions comprising the same.

Further embodiments relate to methods of treating an animal. The methods can include administering to an animal a composition, including a pharmaceutical or an immunogenic composition, such as, a vaccine or immunotherapeutic composition, including those disclosed above and herein. The administering step can include a mode of delivery, such as, for example, transdermal, intranodal, perinodal, oral, intravenous, intradermal, intramuscular, intraperitoneal, mucosal, aerosol inhalation, instillation, and the like. The method can further include a step of assaying to determine a characteristic indicative of a state of a target cell or target cells. The method can include a first assaying step and a second assaying step, wherein the first assaying step precedes the administering step, and wherein the second assaying step follows the administering step. The method can further include a step of comparing the characteristic determined in the first assaying step with the characteristic determined in the second assaying step to obtain a result. The result can be for example, evidence of an immune response, a diminution in number of target cells, a loss of mass or size of a tumor comprising target cells, a decrease in number or concentration of an intracellular parasite infecting target cells, and the like.

Embodiments relate to methods of evaluating immunogenicity of a composition, including a vaccine or an immunotherapeutic composition. The methods can include administering to an animal a vaccine or immunotherapeutic, such as those described above and elsewhere herein, and evaluating immunogenicity based on a characteristic of the animal. The animal can be MHC-transgenic.

Other embodiments relate to methods of evaluating immunogenicity that include *in vitro* stimulation of a T cell with the vaccine or immunotherapeutic composition, such as those described above and elsewhere herein, and evaluating immunogenicity based on a characteristic of the T cell. The stimulation can be a primary stimulation.

Still further embodiments relate to methods of making a passive/adoptive immunotherapeutic. The methods can include combining a T cell or a host cell, such as those described above and elsewhere herein, with a pharmaceutically acceptable adjuvant, carrier, diluent, excipient, and the like.

Other embodiments relate to methods of determining specific T cell frequency, and can include the step of contacting T cells with a MHC-peptide complex comprising an epitope disclosed in Tables 1A or 1B, or a complex comprising a cluster or antigen comprising such an epitope. The contacting step can include at least one feature, such as, for example, immunization, restimulation, detection, enumeration, and the like. The method can further include ELISPOT analysis, limiting dilution analysis, flow cytometry, in situ hybridization, the polymerase chain reaction, any combination thereof, and the like.

Embodiments relate to methods of evaluating immunologic response. The methods can include the above-described methods of determining specific T cell frequency carried out prior to and subsequent to an immunization step.

Other embodiments relate to methods of evaluating immunologic response. The methods can include determining frequency, cytokine production, or cytolytic activity of T cells, prior to and subsequent to a step of stimulation with MHC-peptide complexes comprising an epitope, such as, for example an epitope from Tables 1A or 1B, a cluster or a polypeptide comprising such an epitope.

Further embodiments relate to methods of diagnosing a disease. The methods can include contacting a subject tissue with at least one component, including, for example, a T cell, a host cell, an antibody, a protein, including those described above and elsewhere herein; and diagnosing the disease based on a characteristic of the tissue or of the component. The contacting step can take place *in vivo* or *in vitro*, for example.

Still other embodiments relate to methods of making a composition, including for example, a vaccine. The methods can include combining at least one component. For example, the component can be an epitope, a composition, a construct, a T cell, a host cell; including any of

those described above and elsewhere herein, and the like, with a pharmaceutically acceptable adjuvant, carrier, diluent, excipient, and the like.

Embodiments relate to computer readable media having recorded thereon the sequence of any one of SEQ ID NOS: 108-610, in a machine having a hardware or software that calculates the physical, biochemical, immunologic, molecular genetic properties of a molecule embodying said
5 sequence, and the like.

Still other embodiments relate to methods of treating an animal. The methods can include combining the method of treating an animal that includes administering to the animal a vaccine or immunotherapeutic composition, such as described above and elsewhere herein, combined with at
10 least one mode of treatment, including, for example, radiation therapy, chemotherapy, biochemotherapy, surgery, and the like.

Further embodiments relate to isolated polypeptides that include an epitope cluster. In preferred embodiments the cluster can be from a target-associated antigen having the sequence as disclosed in any one of Tables 68-73, wherein the amino acid sequence includes not more than
15 about 80% of the amino acid sequence of the antigen.

Other embodiments relate to immunogenic compositions, including vaccines or immunotherapeutic products that include an isolated peptide as described above and elsewhere herein. Still other embodiments relate to isolated polynucleotides encoding a polypeptide as described above and elsewhere herein. Other embodiments relate vaccines or immunotherapeutic
20 products that include these polynucleotides. The polynucleotide can be DNA, RNA, and the like.

Still further embodiments relate to kits comprising a delivery device and any of the embodiments mentioned above and elsewhere herein. The delivery device can be a catheter, a syringe, an internal or external pump, a reservoir, an inhaler, microinjector, a patch, and any other like device suitable for any route of delivery. As mentioned, the kit, in addition to the delivery
25 device also includes any of the embodiments disclosed herein. For example, without limitations, the kit can include an isolated epitope, a polypeptide, a cluster, a nucleic acid, an antigen, a pharmaceutical composition that includes any of the foregoing, an antibody, a T cell, a T cell receptor, an epitope-MHC complex, a vaccine, an immunotherapeutic, and the like. The kit can also include items such as detailed instructions for use and any other like item.

30 Brief Description of the Drawings

Figure 1A-1C is a sequence alignment of NY-ESO-1 and several similar protein sequences.

Figure 2 graphically represents a plasmid vaccine backbone useful for delivering nucleic acid-encoded epitopes.

Figures 3A and 3B are FACS profiles showing results of HLA-A2 binding assays for
35 tyrosinase₂₀₇₋₂₁₅ and tyrosinase₂₀₈₋₂₁₆.

Figure 3C shows cytolytic activity against a tyrosinase epitope by human CTL induced by *in vitro* immunization.

Figure 4 is a T=120 min. time point mass spectrum of the fragments produced by proteasomal cleavage of SSX-2₃₁₋₆₈.

5 Figure 5 shows a binding curve for HLA-A2:SSX-2₄₁₋₄₉ with controls.

Figure 6 shows specific lysis of SSX-2₄₁₋₄₉-pulsed targets by CTL from SSX-2₄₁₋₄₉-immunized HLA-A2 transgenic mice.

Figure 7A, B, and C show results of N-terminal pool sequencing of a T=60 min. time point aliquot of the PSMA₁₆₃₋₁₉₂ proteasomal digest.

10 Figure 8 shows binding curves for HLA-A2:PSMA₁₆₈₋₁₇₇ and HLA-A2:PSMA₂₈₈₋₂₉₇ with controls.

Figure 9 shows results of N-terminal pool sequencing of a T=60 min. time point aliquot of the PSMA₂₈₁₋₃₁₀ proteasomal digest.

15 Figure 10 shows binding curves for HLA-A2:PSMA₄₆₁₋₄₆₉, HLA-A2:PSMA₄₆₀₋₄₆₉, and HLA-A2:PSMA₆₆₃₋₆₇₁, with controls.

Figure 11 shows the results of a γ (gamma)-IFN-based ELISPOT assay detecting PSMA₄₆₃₋₄₇₁-reactive HLA-A1⁺ CD8⁺ T cells.

Figure 12 shows blocking of reactivity of the T cells used in figure 10 by anti-HLA-A1 mAb, demonstrating HLA-A1-restricted recognition.

20 Figure 13 shows a binding curve for HLA-A2:PSMA₆₆₃₋₆₇₁, with controls.

Figure 14 shows a binding curve for HLA-A2:PSMA₆₆₂₋₆₇₁, with controls.

Figure 15. Comparison of anti-peptide CTL responses following immunization with various doses of DNA by different routes of injection.

25 Figure 16. Growth of transplanted gp33 expressing tumor in mice immunized by i.ln. injection of gp33 epitope-expressing, or control, plasmid.

Figure 17. Amount of plasmid DNA detected by real-time PCR in injected or draining lymph nodes at various times after i.ln. of i.m. injection, respectively.

Figures 18-70 are proteasomal digestion maps depicting the mapping of mass spectrum peaks from the digest onto the sequence of the indicated substrate.

30 Detailed Description of the Preferred Embodiment

Definitions

Unless otherwise clear from the context of the use of a term herein, the following listed terms shall generally have the indicated meanings for purposes of this description.

35 PROFESSIONAL ANTIGEN-PRESENTING CELL (pAPC) – a cell that possesses T cell costimulatory molecules and is able to induce a T cell response. Well characterized pAPCs include dendritic cells, B cells, and macrophages.

PERIPHERAL CELL – a cell that is not a pAPC.

HOUSEKEEPING PROTEASOME – a proteasome normally active in peripheral cells, and generally not present or not strongly active in pAPCs.

5 IMMUNE PROTEASOME – a proteasome normally active in pAPCs; the immune proteasome is also active in some peripheral cells in infected tissues.

EPITOPE – a molecule or substance capable of stimulating an immune response. In preferred embodiments, epitopes according to this definition include but are not necessarily limited to a polypeptide and a nucleic acid encoding a polypeptide, wherein the polypeptide is capable of stimulating an immune response. In other preferred embodiments, epitopes according to this
10 definition include but are not necessarily limited to peptides presented on the surface of cells, the peptides being non-covalently bound to the binding cleft of class I MHC, such that they can interact with T cell receptors (TCR). Epitopes presented by class I MHC may be in immature or mature form. “Mature” refers to an MHC epitope in distinction to any precursor (“immature”) that may include or consist essentially of a housekeeping epitope, but also includes other sequences in a
15 primary translation product that are removed by processing, including without limitation, alone or in any combination proteasomal digestion, N-terminal trimming, or the action of exogenous enzymatic activities. Thus, a mature epitope may be provided embedded in a somewhat longer polypeptide, the immunological potential of which is due, at least in part, to the embedded epitope; or in its ultimate form that can bind in the MHC binding cleft to be recognized by TCR,
20 respectively.

MHC EPITOPE – a polypeptide having a known or predicted binding affinity for a mammalian class I or class II major histocompatibility complex (MHC) molecule.

HOUSEKEEPING EPITOPE – In a preferred embodiment, a housekeeping epitope is defined as a polypeptide fragment that is an MHC epitope, and that is displayed on a cell in which
25 housekeeping proteasomes are predominantly active. In another preferred embodiment, a housekeeping epitope is defined as a polypeptide containing a housekeeping epitope according to the foregoing definition, that is flanked by one to several additional amino acids. In another preferred embodiment, a housekeeping epitope is defined as a nucleic acid that encodes a housekeeping epitope according to the foregoing definitions.

30 IMMUNE EPITOPE – In a preferred embodiment, an immune epitope is defined as a polypeptide fragment that is an MHC epitope, and that is displayed on a cell in which immune proteasomes are predominantly active. In another preferred embodiment, an immune epitope is defined as a polypeptide containing an immune epitope according to the foregoing definition, that is flanked by one to several additional amino acids. In another preferred embodiment, an immune
35 epitope is defined as a polypeptide including an epitope cluster sequence, having at least two polypeptide sequences having a known or predicted affinity for a class I MHC. In yet another

preferred embodiment, an immune epitope is defined as a nucleic acid that encodes an immune epitope according to any of the foregoing definitions.

TARGET CELL – a cell to be targeted by the vaccines and methods of the invention. Examples of target cells according to this definition include but are not necessarily limited to: a
5 neoplastic cell and a cell harboring an intracellular parasite, such as, for example, a virus, a bacterium, or a protozoan.

TARGET-ASSOCIATED ANTIGEN (TAA) – a protein or polypeptide present in a target cell.

TUMOR-ASSOCIATED ANTIGENS (TuAA) – a TAA, wherein the target cell is a
10 neoplastic cell.

HLA EPITOPE – a polypeptide having a known or predicted binding affinity for a human class I or class II HLA complex molecule.

ANTIBODY – a natural immunoglobulin (Ig), poly- or monoclonal, or any molecule composed in whole or in part of an Ig binding domain, whether derived biochemically or by use of
15 recombinant DNA. Examples include *inter alia*, F(ab), single chain Fv, and Ig variable region-phage coat protein fusions.

ENCODE – an open-ended term such that a nucleic acid encoding a particular amino acid sequence can consist of codons specifying that (poly)peptide, but can also comprise additional sequences either translatable, or for the control of transcription, translation, or replication, or to
20 facilitate manipulation of some host nucleic acid construct.

SUBSTANTIAL SIMILARITY – this term is used to refer to sequences that differ from a reference sequence in an inconsequential way as judged by examination of the sequence. Nucleic acid sequences encoding the same amino acid sequence are substantially similar despite differences in degenerate positions or modest differences in length or composition of any non-coding regions.
25 Amino acid sequences differing only by conservative substitution or minor length variations are substantially similar. Additionally, amino acid sequences comprising housekeeping epitopes that differ in the number of N-terminal flanking residues, or immune epitopes and epitope clusters that differ in the number of flanking residues at either terminus, are substantially similar. Nucleic acids that encode substantially similar amino acid sequences are themselves also substantially similar.

30 FUNCTIONAL SIMILARITY – this term is used to refer to sequences that differ from a reference sequence in an inconsequential way as judged by examination of a biological or biochemical property, although the sequences may not be substantially similar. For example, two nucleic acids can be useful as hybridization probes for the same sequence but encode differing amino acid sequences. Two peptides that induce cross-reactive CTL responses are functionally
35 similar even if they differ by non-conservative amino acid substitutions (and thus do not meet the substantial similarity definition). Pairs of antibodies, or TCRs, that recognize the same epitope can

be functionally similar to each other despite whatever structural differences exist. In testing for functional similarity of immunogenicity one would generally immunize with the “altered” antigen and test the ability of the elicited response (Ab, CTL, cytokine production, etc.) to recognize the target antigen. Accordingly, two sequences may be designed to differ in certain respects while
 5 retaining the same function. Such designed sequence variants are among the embodiments of the present invention.

VACCINE – this term is used to refer to those immunogenic compositions that are capable of eliciting prophylactic and/or therapeutic responses that prevent, cure, or ameliorate disease.

IMMUNOGENIC COMPOSITION - this term is used to refer to compositions capable of
 10 inducing an immune response, a reaction, an effect, and/or an event. In some embodiments, such responses, reactions, effects, and/or events can be induced *in vitro* or *in vivo*, for example. Included among these embodiments are the induction, activation, or expansion of cells involved in cell mediated immunity, for example. One example of such cells is cytotoxic T lymphocytes (CTLs). A vaccine is one type of immunogenic composition. Another example of such a
 15 composition is one that induces, activates, or expands CTLs *in vitro*. Further examples include pharmaceutical compositions and the like.

Table 1A. SEQ ID NOS.* including epitopes in Examples 1-7, 13, 14.

| SEQ ID NO | IDENTITY | SEQUENCE |
|-----------|--------------------|--|
| 1 | Tyr 207-216 | FLPWHRLFLL |
| 2 | Tyrosinase protein | Accession number*: P14679 |
| 3 | SSX-2 protein | Accession number: NP_003138 |
| 4 | PSMA protein | Accession number: NP_004467 |
| 5 | Tyrosinase cDNA | Accession number: NM_000372 |
| 6 | SSX-2 cDNA | Accession number: NM_003147 |
| 7 | PSMA cDNA | Accession number: NM_004476 |
| 8 | Tyr 207-215 | FLPWHRLFL |
| 9 | Tyr 208-216 | LPWHRLFLL |
| 10 | SSX-2 31-68 | YFSKEEWEKMKASEKIFYVYMKRKYEAMTKLGF KATLP |
| 11 | SSX-2 32-40 | FSKEEWEKM |
| 12 | SSX-2 39-47 | KMKASEKIF |
| 13 | SSX-2 40-48 | MKASEKIFY |
| 14 | SSX-2 39-48 | KMKASEKIFY |
| 15 | SSX-2 41-49 | KASEKIFYV |
| 16 | SSX-2 40-49 | MKASEKIFYV |
| 17 | SSX-2 41-50 | KASEKIFYVY |
| 18 | SSX-2 42-49 | ASEKIFYVY |
| 19 | SSX-2 53-61 | RKYEAMTKL |
| 20 | SSX-2 52-61 | KRKYEAMTKL |
| 21 | SSX-2 54-63 | KYEAMTKLGF |
| 22 | SSX-2 55-63 | YEAMTKLGF |
| 23 | SSX-2 56-63 | EAMTKLGF |

| SEQ ID NO | IDENTITY | SEQUENCE |
|-----------|----------------------------|-------------------------------------|
| 24 | HBV18-27 | FLPSDYFPSV |
| 25 | HLA-B44 binder | AEMGKYSFY |
| 26 | SSX-1 41-49 | KYSEKISYV |
| 27 | SSX-3 41-49 | KVSEKIVYV |
| 28 | SSX-4 41-49 | KSSEKIVYV |
| 29 | SSX-5 41-49 | KASEKIIYV |
| 30 | PSMA163-192 | AFSPQGMPEGDLVYVNYARTEDFFKLERDM |
| 31 | PSMA 168-190 | GMPEGDLVYVNYARTEDFFKLER |
| 32 | PSMA 169-177 | MPEGDLVYV |
| 33 | PSMA 168-177 | GMPEGDLVYV |
| 34 | PSMA 168-176 | GMPEGDLVY |
| 35 | PSMA 167-176 | QGMPEGDLVY |
| 36 | PSMA 169-176 | MPEGDLVY |
| 37 | PSMA 171-179 | EGDLVYVNY |
| 38 | PSMA 170-179 | PEGDLVYVNY |
| 39 | PSMA 174-183 | LVYVNYARTE |
| 40 | PSMA 177-185 | VNYARTEDF |
| 41 | PSMA 176-185 | YVNYARTEDF |
| 42 | PSMA 178-186 | NYARTEDFF |
| 43 | PSMA 179-186 | YARTEDFF |
| 44 | PSMA 181-189 | RTEDFFKLE |
| 45 | PSMA 281-310 | RGIAEAVGLPSIPVHPIGYYDAQKLEKMG |
| 46 | PSMA 283-307 | IAEAVGLPSIPVHPIGYYDAQKLE |
| 47 | PSMA 289-297 | LPSIPVHPI |
| 48 | PSMA 288-297 | GLPSIPVHPI |
| 49 | PSMA 297-305 | IGYYDAQKL |
| 50 | PSMA 296-305 | PIGYYDAQKL |
| 51 | PSMA 291-299 | SIPVHPIGY |
| 52 | PSMA 290-299 | PSIPVHPIGY |
| 53 | PSMA 292-299 | IPVHPIGY |
| 54 | PSMA 299-307 | YYDAQKLE |
| 55 | PSMA454-481 | SSIEGNYTLRVDCTPLMYSLVHLTKEL |
| 56 | PSMA 456-464 | IEGNYTLRV |
| 57 | PSMA 455-464 | SIEGNYTLRV |
| 58 | PSMA 457-464 | EGNYTLRV |
| 59 | PSMA 461-469 | TLRVDCTPL |
| 60 | PSMA 460-469 | YTLRVDCTPL |
| 61 | PSMA 462-470 | LRVDCTPLM |
| 62 | PSMA 463-471 | RVDCTPLMY |
| 63 | PSMA 462-471 | LRVDCTPLMY |
| 64 | PSMA653-687 | FDKSNPIVLRMMNDQLMFLERAFIDPLGLPDRPFY |
| 65 | PSMA 660-681 | VLRMMNDQLMFLERAFIDPLGL |
| 66 | PSMA 663-671 | MMNDQLMFL |
| 67 | PSMA 662-671 | RMMNDQLMFL |
| 68 | PSMA 662-670 | RMMNDQLMF |
| 69 | Tyr 1-17 | MLLAVLYCLLWSFQTSA |
| 70 | GP100 protein ² | Accession number: P40967 |
| 71 | MAGE-1 protein | Accession number: P43355 |
| 72 | MAGE-2 protein | Accession number: P43356 |

| SEQ ID NO | IDENTITY | SEQUENCE |
|-----------|----------------------------|-----------------------------|
| 73 | MAGE-3 protein | Accession number: P43357 |
| 74 | NY-ESO-1 protein | Accession number: P78358 |
| 75 | LAGE-1a protein | Accession number: CAA11116 |
| 76 | LAGE-1b protein | Accession number: CAA11117 |
| 77 | PRAME protein | Accession number: NP 006106 |
| 78 | PSA protein | Accession number: P07288 |
| 79 | PSCA protein | Accession number: O43653 |
| 80 | GP100 cds | Accession number: U20093 |
| 81 | MAGE-1 cds | Accession number: M77481 |
| 82 | MAGE-2 cds | Accession number: L18920 |
| 83 | MAGE-3 cds | Accession number: U03735 |
| 84 | NY-ESO-1 cDNA | Accession number: U87459 |
| 85 | PRAME cDNA | Accession number: NM 006115 |
| 86 | PSA cDNA | Accession number: NM 001648 |
| 87 | PSCA cDNA | Accession number: AF043498 |
| 88 | CEA protein | Accession number: P06731 |
| 89 | CEA cDNA | Accession number: NM 004363 |
| 90 | Her2/Neu protein | Accession number: P04626 |
| 91 | Her2/Neu cDNA | Accession number: M11730 |
| 92 | SCP-1 protein | Accession number: Q15431 |
| 93 | SCP-1 cDNA | Accession number: X95654 |
| 94 | SSX-4 protein | Accession number: O60224 |
| 95 | SSX-4 cDNA | Accession number: NM 005636 |
| 96 | GAGE-1 protein | Accession number: Q13065 |
| 97 | GAGE-1 cDNA | Accession number: U19142 |
| 98 | Suvinin protein | Accession number: O15392 |
| 99 | Survivin cDNA | Accession number: NM 001168 |
| 100 | Melan-A protein | Accession number: Q16655 |
| 101 | Melan-A cDNA | Accession number: U06452 |
| 102 | BAGE protein | Accession number: Q13072 |
| 103 | BAGE cDNA | Accession number: U19180 |
| 104 | PSA 59-67 | WVLTAAHCI |
| 105 | Glandular Kallikrein 1 | Accession number: P06870 |
| 106 | Elastase 2A | Accession number: P08217 |
| 107 | Pancreatic elastase IIB | Accession number: NP_056933 |

Table 1B. SEQ ID NOS.* including epitopes in Examples 15-67.

| SEQ ID NO | IDENTITY | SEQUENCE |
|-----------|-------------|-------------|
| 108 | Tyr 171-179 | NIYDLFVWM |
| 109 | Tyr 173-182 | YDLFVWMHY Y |
| 110 | Tyr 174-182 | DLFVWMHY Y |
| 111 | Tyr 186-194 | DALLGGSEI |
| 112 | Tyr 191-200 | GSEIWRDIDF |
| 113 | Tyr 192-200 | SEIWRDIDF |
| 114 | Tyr 193-201 | EIWRDIDFA |

| SEQ ID NO | IDENTITY | SEQUENCE |
|-----------|-------------|------------|
| 115 | Tyr 407-416 | LQEVYPEANA |
| 116 | Tyr 409-418 | EVYPEANAPI |
| 117 | Tyr 410-418 | VYPEANAPI |
| 118 | Tyr 411-418 | YPEANAPI |
| 119 | Tyr 411-420 | YPEANAPIGH |
| 120 | Tyr 416-425 | APIGHNRESY |
| 121 | Tyr 417-425 | PIGHNRESY |
| 122 | Tyr 417-426 | PIGHNRESYM |
| 123 | Tyr 416-425 | APIGHNRESY |
| 124 | Tyr 417-425 | PIGHNRESY |
| 125 | Tyr 423-430 | ESYMPVFI |
| 126 | Tyr 423-432 | ESYMPVFIPL |
| 127 | Tyr 424-432 | SYMPVFIPL |
| 128 | Tyr 424-433 | SYMPVFIPLY |
| 129 | Tyr 425-433 | YMPVFIPLY |
| 130 | Tyr 426-434 | MVPFIPLYR |
| 131 | Tyr 426-435 | MVPFIPLYRN |
| 132 | Tyr 427-434 | VFPFIPLYR |
| 133 | Tyr 430-437 | IPLYRNGD |
| 134 | Tyr 430-439 | IPLYRNGDFF |
| 135 | Tyr 431-439 | PLYRNGDFF |
| 136 | Tyr 431-440 | PLYRNGDFFI |
| 137 | Tyr 434-443 | RNGDFFISSK |
| 138 | Tyr 435-443 | NGDFFISSK |
| 139 | Tyr 463-471 | YIKSYLEQA |
| 140 | Tyr 466-474 | SYLEQASRI |
| 141 | Tyr 469-478 | EQASRIWSWL |
| 142 | Tyr 470-478 | QASRIWSWL |
| 143 | Tyr 471-478 | ASRIWSWL |
| 144 | Tyr 471-479 | ASRIWSWLL |
| 145 | Tyr 473-481 | RIWSWLLGA |
| 146 | CEA 92-100 | GPAYSGREI |
| 147 | CEA 92-101 | GPAYSGREII |
| 148 | CEA 93-100 | PAYSGREI |
| 149 | CEA 93-101 | PAYSGREII |
| 150 | CEA 93-102 | PAYSGREIYY |
| 151 | CEA 94-102 | AYSGREIYY |
| 152 | CEA 97-105 | GREIYPNA |
| 153 | CEA 98-107 | REIYPNASL |
| 154 | CEA 99-107 | EIYPNASL |
| 155 | CEA 99-108 | EIYPNASLL |
| 156 | CEA 100-107 | IYPNASL |
| 157 | CEA 100-108 | IYPNASLL |
| 158 | CEA 100-109 | IYPNASLLI |
| 159 | CEA 102-109 | YPNASLLI |
| 160 | CEA 107-116 | LLIQNIQND |
| 161 | CEA 132-141 | EEATGQFRVY |
| 162 | CEA 133-141 | EATGQFRVY |
| 163 | CEA 141-149 | YPELPKPSI |

| SEQ ID NO | IDENTITY | SEQUENCE |
|-----------|-------------|-------------|
| 164 | CEA 142-149 | PELPKPSI |
| 165 | CEA 225-233 | RSDSVILNV |
| 166 | CEA 225-234 | RSDSVILNVL |
| 167 | CEA 226-234 | SDSVILNVL |
| 168 | CEA 226-235 | SDSVILNVLY |
| 169 | CEA 227-235 | DSVILNVLY |
| 170 | CEA 233-242 | VLYGPDAPTI |
| 171 | CEA 234-242 | LYGPDAPTI |
| 172 | CEA 235-242 | YGPDAPI |
| 173 | CEA 236-245 | GPDAPTISPL |
| 174 | CEA 237-245 | PDAPTISPL |
| 175 | CEA 238-245 | DAPTISPL |
| 176 | CEA 239-247 | APTISPLNT |
| 177 | CEA 240-249 | PTISPLNTSY |
| 178 | CEA 241-249 | TISPLNTSY |
| 179 | CEA 240-249 | PTISPLNTSY |
| 180 | CEA 241-249 | TISPLNTSY |
| 181 | CEA 246-255 | NTSYRSGENL |
| 182 | CEA 247-255 | TSYRSGENL |
| 183 | CEA 248-255 | SYRSGENL |
| 184 | CEA 248-257 | SYRSGENLNL |
| 185 | CEA 249-257 | YRSGENLNL |
| 186 | CEA 251-259 | SGENLNLSC |
| 187 | CEA 253-262 | ENLNLSCHAA |
| 188 | CEA 254-262 | NLNLSCHAA |
| 189 | CEA 260-269 | HAASNPPAQY |
| 190 | CEA 261-269 | AASNPPAQY |
| 191 | CEA 264-273 | NPPAQYSWFV |
| 192 | CEA 265-273 | PPAQYSWFV |
| 193 | CEA 266-273 | PAQYSWFV |
| 194 | CEA 272-280 | FVNGTFQQS |
| 195 | CEA 310-319 | RTTVTTITVY |
| 196 | CEA 311-319 | TTVTTITVY |
| 197 | CEA 319-327 | YAEPKPFIT |
| 198 | CEA 319-328 | YAEPKPFIT |
| 199 | CEA 320-327 | AEPPKPFIT |
| 200 | CEA 321-328 | EPPKPFIT |
| 201 | CEA 321-329 | EPPKPFITS |
| 202 | CEA 322-329 | PPKPFITS |
| 203 | CEA 382-391 | SVTRNDVGOPY |
| 204 | CEA 383-391 | VTRNDVGOPY |
| 205 | CEA 389-397 | GPYECGIQN |
| 206 | CEA 391-399 | YECGIQNEL |
| 207 | CEA 394-402 | GIGNELSVD |
| 208 | CEA 403-411 | HSDPVILNV |
| 209 | CEA 403-412 | HSDPVILNVL |
| 210 | CEA 404-412 | SDPVILNVL |
| 211 | CEA 404-413 | SDPVILNVLY |
| 212 | CEA 405-412 | DPVILNVL |

| SEQ ID NO | IDENTITY | SEQUENCE |
|-----------|-------------|------------|
| 213 | CEA 405-413 | DPVILNVLY |
| 214 | CEA 408-417 | ILNVLYGPDD |
| 215 | CEA 411-420 | VLYGPDDPTI |
| 216 | CEA 412-420 | LYGPDDPTI |
| 217 | CEA 413-420 | YGPDDPTI |
| 218 | CEA 417-425 | DPTISPSYT |
| 219 | CEA 418-427 | PTISPSYTTY |
| 220 | CEA 419-427 | TISPSYTTY |
| 221 | CEA 418-427 | PTISPSYTTY |
| 222 | CEA 419-427 | TISPSYTTY |
| 223 | CEA 419-428 | TISPSYTTYR |
| 224 | CEA 424-433 | YTYRPGVNL |
| 225 | CEA 425-433 | TYRPGVNL |
| 226 | CEA 426-433 | YYRPGVNL |
| 227 | CEA 426-435 | YYRPGVNL |
| 228 | CEA 427-435 | YRPGVNL |
| 229 | CEA 428-435 | RPGVNL |
| 230 | CEA 428-437 | RPGVNL |
| 231 | CEA 430-438 | GVNLSLSCH |
| 232 | CEA 431-440 | VNLSLSCHAA |
| 233 | CEA 432-440 | NLSLSCHAA |
| 234 | CEA 438-447 | HAASNPPAQY |
| 235 | CEA 439-447 | AASNPPAQY |
| 236 | CEA 442-451 | NPPAQYSWLI |
| 237 | CEA 443-451 | PPAQYSWLI |
| 238 | CEA 444-451 | PAQYSWLI |
| 239 | CEA 449-458 | WLIDGNIQQH |
| 240 | CEA 450-458 | LIDGNIQQH |
| 241 | CEA 450-459 | LIDGNIQQHT |
| 242 | CEA 581-590 | RSDPVTLDVL |
| 243 | CEA 582-590 | SDPVTLDVL |
| 244 | CEA 582-591 | SDPVTLDVLY |
| 245 | CEA 583-590 | DPVTLDVL |
| 246 | CEA 583-591 | DPVTLDVLY |
| 247 | CEA 588-597 | DVLYGPDPTI |
| 248 | CEA 589-597 | VLYGPDPTI |
| 249 | CEA 596-605 | PIISPPDSSY |
| 250 | CEA 597-605 | IISPPDSSY |
| 251 | CEA 597-606 | IISPPDSSYL |
| 252 | CEA 599-606 | SPPDSSYL |
| 253 | CEA 600-608 | PPDSSYLSG |
| 254 | CEA 600-609 | PPDSSYLSGA |
| 255 | CEA 602-611 | DSSYLSGANL |
| 256 | CEA 603-611 | SSYLSGANL |
| 257 | CEA 604-613 | SYLSGANLNL |
| 258 | CEA 605-613 | YLSGANLNL |
| 259 | CEA 610-618 | NLNLSCHSA |
| 260 | CEA 620-629 | NPSPQYSWRI |
| 261 | CEA 622-629 | SPQYSWRI |

| SEQ ID NO | IDENTITY | SEQUENCE |
|-----------|----------------|------------|
| 262 | CEA 627-635 | WRINGIPQQ |
| 263 | CEA 628-636 | RINGIPQQH |
| 264 | CEA 628-637 | RINGIPQQHT |
| 265 | CEA 631-639 | GIPQQHTQV |
| 266 | CEA 632-639 | IPQQHTQV |
| 267 | CEA 644-653 | KITPNNGTY |
| 268 | CEA 645-653 | ITPNNGTY |
| 269 | CEA 647-656 | PNNGTYACF |
| 270 | CEA 648-656 | NNNGTYACF |
| 271 | CEA 650-657 | NGTYACFV |
| 272 | CEA 661-670 | ATGRNNSIVK |
| 273 | CEA 662-670 | TGRNNSIVK |
| 274 | CEA 664-672 | RNNSIVKSI |
| 275 | CEA 666-674 | NSIVKSITV |
| 276 | GAGE-1 7-16 | STYRPRPRRY |
| 277 | GAGE-1 8-16 | TYRPRPRRY |
| 278 | GAGE-1 10-18 | RPRPRRYVE |
| 279 | GAGE-1 16-23 | YVEPPEMI |
| 280 | GAGE-1 22-31 | MIGPMRPEQF |
| 281 | GAGE-1 23-31 | IGPMRPEQF |
| 282 | GAGE-1 24-31 | GPMRPEQF |
| 283 | GAGE-1 105-114 | KTPPEEMRSH |
| 284 | GAGE-1 106-115 | TPEEEMRSHY |
| 285 | GAGE-1 107-115 | PEEEMRSHY |
| 286 | GAGE-1 110-119 | EMRSHYVAQT |
| 287 | GAGE-1 113-121 | SHYVAQTGI |
| 288 | GAGE-1 115-124 | YVAQTGILWL |
| 289 | GAGE-1 116-124 | VAQTGILWL |
| 290 | GAGE-1 116-125 | VAQTGILWLL |
| 291 | GAGE-1 117-125 | AQTGILWLL |
| 292 | GAGE-1 118-126 | QTGILWLLM |
| 293 | GAGE-1 118-127 | QTGILWLLMN |
| 294 | GAGE-1 120-129 | GILWLLMNNC |
| 295 | GAGE-1 121-129 | ILWLLMNNC |
| 296 | GAGE-1 124-131 | LLMNNCFL |
| 297 | GAGE-1 123-131 | WLLMNNCFL |
| 298 | GAGE-1 122-130 | LWLLMNNCF |
| 299 | GAGE-1 121-130 | ILWLLMNNCF |
| 300 | GAGE-1 121-129 | ILWLLMNNC |
| 301 | GAGE-1 120-129 | GILWLLMNNC |
| 302 | GAGE-1 118-127 | QTGILWLLMN |
| 303 | GAGE-1 118-126 | QTGILWLLM |
| 304 | GAGE-1 117-125 | AQTGILWLL |
| 305 | GAGE-1 116-125 | VAQTGILWLL |
| 306 | GAGE-1 116-124 | VAQTGILWL |
| 307 | GAGE-1 115-124 | YVAQTGILWL |
| 308 | GAGE-1 113-121 | SHYVAQTGI |
| 309 | MAGE-1 62-70 | SAFPTTINF |
| 310 | MAGE-1 61-70 | ASAFPTTINF |

| SEQ ID NO | IDENTITY | SEQUENCE |
|-----------|----------------|------------|
| 311 | MAGE-1 60-68 | GASAFPTTI |
| 312 | MAGE-1 57-66 | SPQGASAFPT |
| 313 | MAGE-1 144-151 | FGKASESL |
| 314 | MAGE-1 143-151 | IFGKASESL |
| 315 | MAGE-1 142-151 | EIFGKASESL |
| 316 | MAGE-1 142-149 | EIFGKASE |
| 317 | MAGE-1 133-140 | IKNYKHCF |
| 318 | MAGE-1 132-140 | VIKNYKHCF |
| 319 | MAGE-1 131-140 | SVIKNYKHCF |
| 320 | MAGE-1 132-139 | VIKNYKHC |
| 321 | MAGE-1 131-139 | SVIKNYKHC |
| 322 | MAGE-1 128-136 | MLESVIKNY |
| 323 | MAGE-1 127-136 | EMLESVIKNY |
| 324 | MAGE-1 126-134 | AEMLESVIK |
| 325 | MAGE-2 274-283 | GPRALIETSY |
| 326 | MAGE-2 275-283 | PRALIETSY |
| 327 | MAGE-2 276-284 | RALIETSYV |
| 328 | MAGE-2 277-286 | ALIETSYVKV |
| 329 | MAGE-2 278-286 | LIETSYVKV |
| 330 | MAGE-2 278-287 | LIETSYVKVL |
| 331 | MAGE-2 279-287 | IETSYVKVL |
| 332 | MAGE-2 280-289 | ETSYVKVLHH |
| 333 | MAGE-2 282-291 | SYVKVLHHTL |
| 334 | MAGE-2 283-291 | YVKVLHHTL |
| 335 | MAGE-2 285-293 | KVLHHTLKI |
| 336 | MAGE-2 303-311 | PLHERALRE |
| 337 | MAGE-2 302-309 | PPLHERAL |
| 338 | MAGE-2 301-309 | YPPLHERAL |
| 339 | MAGE-2 300-309 | SYPLHERAL |
| 340 | MAGE-2 299-307 | ISYPPLHER |
| 341 | MAGE-2 298-307 | HISYPPLHER |
| 342 | MAGE-2 292-299 | KIGGEPHI |
| 343 | MAGE-2 291-299 | LKIGGEPHI |
| 344 | MAGE-2 290-299 | TLKIGGEPHI |
| 345 | MAGE-3 303-311 | PLHEWVLRE |
| 346 | MAGE-3 302-309 | PPLHEWVL |
| 347 | MAGE-3 301-309 | YPPLHEWVL |
| 348 | MAGE-3 301-308 | YPPLHEWV |
| 349 | MAGE-3 300-308 | SYPLHEWV |
| 350 | MAGE-3 299-308 | ISYPPLHEWV |
| 351 | MAGE-3 298-307 | HISYPPLHEW |
| 352 | MAGE-3 293-301 | ISGGPHISY |
| 353 | MAGE-3 292-301 | KISGGPHISY |
| 354 | Melan-A 45-54 | CWYCRRRNGY |
| 355 | Melan-A 46-54 | WYCRRRNGY |
| 356 | Melan-A 47-55 | YCRRRNGYR |
| 357 | Melan-A 49-57 | RRRNGYRAL |
| 358 | Melan-A 51-60 | RNGYRALMDK |
| 359 | Melan-A 52-60 | NGYRALMDK |

| SEQ ID NO | IDENTITY | SEQUENCE |
|-----------|---------------|-------------|
| 360 | Melan-A 55-63 | RALMDKSLH |
| 361 | Melan-A 56-63 | ALMDKSLH |
| 362 | Melan-A 55-64 | RALMDKSLHV |
| 363 | Melan-A 56-64 | ALMDKSLHV |
| 364 | PRAME 275-284 | YISPEKEEQY |
| 365 | PRAME 276-284 | ISPEKEEQY |
| 366 | PRAME 277-285 | SPEKEEQYI |
| 367 | PRAME 278-285 | PEKEEQYI |
| 368 | PRAME 279-288 | EKEEQYIAQF |
| 369 | PRAME 280-288 | KEEQYIAQF |
| 370 | PRAME 283-292 | QYIAQFTSQF |
| 371 | PRAME 284-292 | YIAQFTSQF |
| 372 | PRAME 284-293 | YIAQFTSQFL |
| 373 | PRAME 285-293 | IAQFTSQFL |
| 374 | PRAME 286-295 | AQFTSQFLSL |
| 375 | PRAME 287-295 | QFTSQFLSL |
| 376 | PRAME 290-298 | SQFLSLQCL |
| 377 | PRAME 439-448 | VLYPVPLESY |
| 378 | PRAME 440-448 | LYPVPLESY |
| 379 | PRAME 446-455 | ESYEDIHGTL |
| 380 | PRAME 448-457 | YEDIHGTLHL |
| 381 | PRAME 449-457 | EDIHGTLHL |
| 382 | PRAME 451-460 | IHGTLHLERL |
| 383 | PRAME 454-463 | TLHLERLAYL |
| 384 | PRAME 455-463 | LHLERLAYL |
| 385 | PRAME 456-463 | HLEERLAYL |
| 386 | PRAME 456-465 | HLEERLAYLHA |
| 387 | PRAME 458-467 | ERLAYLHARL |
| 388 | PRAME 459-467 | RLAYLHARL |
| 389 | PRAME 459-468 | RLAYLHARLR |
| 390 | PRAME 460-467 | LAYLHARL |
| 391 | PRAME 460-468 | LAYLHARLR |
| 392 | PRAME 461-470 | AYLHARLREL |
| 393 | PRAME 462-470 | YLHARLREL |
| 394 | PRAME 462-471 | YLHARLRELL |
| 395 | PRAME 463-471 | LHARLRELL |
| 396 | PRAME 464-471 | HARLRELL |
| 397 | PRAME 464-472 | HARLRELLC |
| 398 | PRAME 469-478 | ELLCGLGRPS |
| 399 | PRAME 470-478 | LLCGLGRPS |
| 400 | PSA 144-153 | QEPALGTTCTY |
| 401 | PSA 145-153 | EPALGTTCTY |
| 402 | PSA 162-171 | PEEFLTPKKL |
| 403 | PSA 163-171 | EEFLTPKKL |
| 404 | PSA 165-173 | FLTPKKLQOC |
| 405 | PSA 165-174 | FLTPKKLQOCV |
| 406 | PSA 166-174 | LTPKKLQOCV |
| 407 | PSA 167-174 | TPKKLQOCV |
| 408 | PSA 167-175 | TPKKLQOCVD |

| SEQ ID NO | IDENTITY | SEQUENCE |
|-----------|---------------|------------|
| 409 | PSA 170-179 | KLQCVDLHVI |
| 410 | PSA 171-179 | LQCVDLHVI |
| 411 | PSCA 73-81 | DSQDYYVGK |
| 412 | PSCA 74-82 | SQDYYVGKK |
| 413 | PSCA 74-83 | SQDYYVGKKN |
| 414 | PSCA 76-84 | DYYVGKKNI |
| 415 | PSCA 77-84 | YYVGKKNI |
| 416 | PSCA 78-86 | YVGKKNITC |
| 417 | PSCA 78-87 | YVGKKNITCC |
| 418 | PSMA 381-390 | WVFGGIDPQS |
| 419 | PSMA 385-394 | GIDPQSGAAV |
| 420 | PSMA 386-394 | IDPQSGAAV |
| 421 | PSMA 387-394 | DPQSGAAV |
| 422 | PSMA 387-395 | DPQSGAAVV |
| 423 | PSMA 387-396 | DPQSGAAVVH |
| 424 | PSMA 388-396 | PQSGAAVVH |
| 425 | PSMA 389-398 | QSGAAVVHEI |
| 426 | PSMA 390-398 | SGAAVVHEI |
| 427 | PSMA 391-398 | GAAVVHEI |
| 428 | PSMA 391-399 | GAAVVHEIV |
| 429 | PSMA 392-399 | AAVVHEIV |
| 430 | PSMA 597-605 | CRDYAVVLR |
| 431 | PSMA 598-607 | RDYAVVLRKY |
| 432 | PSMA 599-607 | DYAVVLRKY |
| 433 | PSMA 600-607 | YAVVLRKY |
| 434 | PSMA 602-611 | VVLRKYADKI |
| 435 | PSMA 603-611 | VLRKYADKI |
| 436 | PSMA 603-612 | VLRKYADKIY |
| 437 | PSMA 604-611 | LRKYADKI |
| 438 | PSMA 604-612 | LRKYADKIY |
| 439 | PSMA 605-614 | RKYADKIYSI |
| 440 | PSMA 606-614 | KYADKIYSI |
| 441 | PSMA 607-614 | YADKIYSI |
| 442 | PSMA 616-625 | MKHPQEMKTY |
| 443 | PSMA 617-625 | KHPQEMKTY |
| 444 | PSMA 618-627 | HPQEMKTYSV |
| 445 | SCP-1 62-71 | IDSDPALQKV |
| 446 | SCP-1 63-71 | DSDPALQKV |
| 447 | SCP-1 67-76 | ALQKVNFLPV |
| 448 | SCP-1 70-78 | KVNFLPVLE |
| 449 | SCP-1 71-80 | VNFLPVLEQV |
| 450 | SCP-1 72-80 | NFLPVLEQV |
| 451 | SCP-1 75-84 | PVLEQVGNSD |
| 452 | SCP-1 76-84 | VLEQVGNSD |
| 453 | SCP-1 202-210 | YEREETRQV |
| 454 | SCP-1 202-211 | YEREETRQVY |
| 455 | SCP-1 203-211 | EREETRQVY |
| 456 | SCP-1 203-212 | EREETRQVYM |
| 457 | SCP-1 204-212 | REETRQVYM |

| SEQ ID NO | IDENTITY | SEQUENCE |
|-----------|---------------|------------|
| 458 | SCP-1 211-220 | YMDLNSNIEK |
| 459 | SCP-1 213-221 | DLNSNIEKM |
| 460 | SCP-1 216-226 | SNIEKMITAF |
| 461 | SCP-1 217-225 | NIEKMITAF |
| 462 | SCP-1 218-225 | IEKMITAF |
| 463 | SCP-1 397-406 | RLENYEDQLI |
| 464 | SCP-1 398-406 | LENYEDQLI |
| 465 | SCP-1 398-407 | LENYEDQLII |
| 466 | SCP-1 399-407 | ENYEDQLII |
| 467 | SCP-1 399-408 | ENYEDQLIIL |
| 468 | SCP-1 400-408 | NYEDQLIIL |
| 469 | SCP-1 400-409 | NYEDQLIILT |
| 470 | SCP-1 401-409 | YEDQLIILT |
| 471 | SCP-1 401-410 | YEDQLIILTM |
| 472 | SCP-1 402-410 | EDQLIILTM |
| 473 | SCP-1 406-415 | IILTMELQKT |
| 474 | SCP-1 407-415 | ILTMELQKT |
| 475 | SCP-1 424-432 | KLTNNKEVE |
| 476 | SCP-1 424-433 | KLTNNKEVEL |
| 477 | SCP-1 425-433 | LTNNKEVEL |
| 478 | SCP-1 429-438 | KEVELEELKK |
| 479 | SCP-1 430-438 | EVELEELKK |
| 480 | SCP-1 430-439 | EVELEELKKV |
| 481 | SCP-1 431-439 | VELEELKKV |
| 482 | SCP-1 530-539 | ETSDMTLELK |
| 483 | SCP-1 531-539 | TSDMTLELK |
| 484 | SCP-1 548-556 | NKKQEERML |
| 485 | SCP-1 553-562 | ERMLTQIENL |
| 486 | SCP-1 554-562 | RMLTQIENL |
| 487 | SCP-1 555-562 | MLTQIENL |
| 488 | SCP-1 555-564 | MLTQIENLQE |
| 489 | SCP-1 560-569 | ENLQETETQL |
| 490 | SCP-1 561-569 | NLQETETQL |
| 491 | SCP-1 561-570 | NLQETETQLR |
| 492 | SCP-1 567-576 | TQLRNELEYV |
| 493 | SCP-1 568-576 | QLRNELEYV |
| 494 | SCP-1 571-580 | NELEYVREEL |
| 495 | SCP-1 572-580 | ELEYVREEL |
| 496 | SCP-1 573-580 | LEYVREEL |
| 497 | SCP-1 574-583 | EYVREELKQK |
| 498 | SCP-1 575-583 | YVREELKQK |
| 499 | SCP-1 675-684 | LLEEVEKAKV |
| 500 | SCP-1 676-684 | LEEVEKAKV |
| 501 | SCP-1 676-685 | LEEVEKAKVI |
| 502 | SCP-1 677-685 | EEVEKAKVI |
| 503 | SCP-1 681-690 | KAKVIADAEV |
| 504 | SCP-1 683-692 | KVIADAEVKL |
| 505 | SCP-1 684-692 | VIADAEVKL |
| 506 | SCP-1 685-692 | IADAEVKL |

| SEQ ID NO | IDENTITY | SEQUENCE |
|-----------|---------------|------------|
| 507 | SCP-1 694-702 | KEIDKRCQH |
| 508 | SCP-1 694-703 | KEIDKRCQHK |
| 509 | SCP-1 695-703 | EIDKRCQHK |
| 510 | SCP-1 695-704 | EIDKRCQHKI |
| 511 | SCP-1 696-704 | IDKRCQHKI |
| 512 | SCP-1 697-704 | DKRCQHKI |
| 513 | SCP-1 698-706 | KRCQHKIAE |
| 514 | SCP-1 698-707 | KRCQHKIAEM |
| 515 | SCP-1 699-707 | RCQHKIAEM |
| 516 | SCP-1 701-710 | QHKIAEMVAL |
| 517 | SCP-1 702-710 | HKIAEMVAL |
| 518 | SCP-1 703-710 | KIAEMVAL |
| 519 | SCP-1 737-746 | QEQSSLRASL |
| 520 | SCP-1 738-746 | EQSSLRASL |
| 521 | SCP-1 739-746 | QSSLRASL |
| 522 | SCP-1 741-750 | SLRASLEIEL |
| 523 | SCP-1 742-750 | LRASLEIEL |
| 524 | SCP-1 743-750 | RASLEIEL |
| 525 | SCP-1 744-753 | ASLEIELSNL |
| 526 | SCP-1 745-753 | SLEIELSNL |
| 527 | SCP-1 745-754 | SLEIELSNLK |
| 528 | SCP-1 746-754 | LEIELSNLK |
| 529 | SCP-1 747-755 | EIELSNLKA |
| 530 | SCP-1 749-758 | ELSNLKAELL |
| 531 | SCP-1 750-758 | LSNLKAELL |
| 532 | SCP-1 751-760 | SNLKAELLSV |
| 533 | SCP-1 752-760 | NLKAELLSV |
| 534 | SCP-1 752-761 | NLKAELLSVK |
| 535 | SCP-1 753-761 | LKAELLSVK |
| 536 | SCP-1 753-762 | LKAELLSVKK |
| 537 | SCP-1 754-762 | KAELLSVKK |
| 538 | SCP-1 755-763 | AELLSVKKQ |
| 539 | SCP-1 787-796 | EKKDKKTQTF |
| 540 | SCP-1 788-796 | KKDKKTQTF |
| 541 | SCP-1 789-796 | KDKKTQTF |
| 542 | SCP-1 797-806 | LLETPDIYWK |
| 543 | SCP-1 798-806 | LETPDIYWK |
| 544 | SCP-1 798-807 | LETPDIYWKL |
| 545 | SCP-1 799-807 | ETPDYIYWK |
| 546 | SCP-1 800-807 | TPDIYWK |
| 547 | SCP-1 809-817 | SKAVPSQTV |
| 548 | SCP-1 810-817 | KAVPSQTV |
| 549 | SCP-1 812-821 | VPSQTVSRNF |
| 550 | SCP-1 815-824 | QTVSRNFTSV |
| 551 | SCP-1 816-824 | TVSRNFTSV |
| 552 | SCP-1 816-825 | TVSRNFTSVD |
| 553 | SCP-1 823-832 | SVDHGISKDK |
| 554 | SCP-1 829-838 | SKDKRDYLWT |
| 555 | SCP-1 832-840 | KRDYLWISA |

| SEQ ID NO | IDENTITY | SEQUENCE |
|-----------|------------------|------------------------------------|
| 556 | SCP-1 832-841 | KRDYLWTS AK |
| 557 | SCP-1 833-841 | RDYLWTS AK |
| 558 | SCP-1 835-843 | YLWTS AKNT |
| 559 | SCP-1 835-844 | YLWTS AKNTL |
| 560 | SCP-1 837-844 | WTS AKNTL |
| 561 | SCP-1 841-850 | KNTLSTPLPK |
| 562 | SCP-1 842-850 | NTLSTPLPK |
| 563 | SCP-1 832-840 | KRDYLWTS A |
| 564 | SCP-1 832-841 | KRDYLWTS AK |
| 565 | SCP-1 833-841 | RDYLWTS AK |
| 566 | SCP-1 835-843 | YLWTS AKNT |
| 567 | SCP-1 839-846 | SAKNTLST |
| 568 | SCP-1 841-850 | KNTLSTPLPK |
| 569 | SCP-1 842-850 | NTLSTPLPK |
| 570 | SCP-1 843-852 | TLSTPLPKAY |
| 571 | SCP-1 844-852 | LSTPLPKAY |
| 572 | SSX-2 5-12 | DAFARRPT |
| 573 | SSX-2 7-15 | FARRPTVGA |
| 574 | SSX-2 8-17 | ARRPTVGAQI |
| 575 | SSX-2 9-17 | RRPTVGAQI |
| 576 | SSX-2 10-17 | RPTVGAQI |
| 577 | SSX-2 13-21 | VGAQIPEKI |
| 578 | SSX-2 14-21 | GAQIPEKI |
| 579 | SSX-2 15-24 | AQIPEKIQKA |
| 580 | SSX-2 16-24 | QIPEKIQKA |
| 581 | SSX-2 16-25 | QIPEKIQKAF |
| 582 | SSX-2 17-24 | IPEKIQKA |
| 583 | SSX-2 17-25 | IPEKIQKAF |
| 584 | SSX-2 18-25 | PEKIQKAF |
| 585 | Survivin 116-124 | ETNNKKKEF |
| 586 | Survivin 117-124 | TNNKKKEF |
| 587 | Survivin 122-131 | KEFEETAKKV |
| 588 | Survivin 123-131 | EFEETAKKV |
| 589 | Survivin 127-134 | TAKKVRRRA |
| 590 | Survivin 126-134 | ETAKKVRRRA |
| 591 | Survivin 128-136 | AKKVRRRAIE |
| 592 | Survivin 129-138 | KKVRRRAIEQL |
| 593 | Survivin 130-138 | KVRRRAIEQL |
| 594 | Survivin 130-139 | KVRRRAIEQLA |
| 595 | Survivin 131-138 | VRRRAIEQL |
| 596 | BAGE 24-31 | SPVVSWRL |
| 597 | BAGE 21-29 | KEESPVVSW |
| 598 | BAGE 19-27 | LMKEESPVV |
| 599 | BAGE 18-27 | RLMKEESPVV |
| 600 | BAGE 18-26 | RLMKEESPV |
| 601 | BAGE 14-22 | LLQARLMKE |
| 602 | BAGE 13-22 | QLLQARLMKE |
| 603 | Survivin 13-28 | FLKDHRISTFKNWPFL |
| 604 | Survivin 79-111 | KHSSGCAFLSVKKQFEELTLGEFLKLDREERAKN |

| SEQ ID NO | IDENTITY | SEQUENCE |
|-----------|------------------|----------------------------|
| 605 | Survivin 130-141 | KVRRRAIEQLAAM |
| 606 | GAGE-1 116-133 | VAQTGILWLLMNNCFLNL |
| 607 | BAGE 7-17 | FLALSAQLLQA |
| 608 | BAGE 18-27 | RLMKEESPVV |
| 609 | BAGE 2-27 | AARAVFLALSAQLLQARLMKEESPVV |
| 610 | BAGE 30-39 | RLEPEDGTAL |

*Any of SEQ ID NOS. 108-602 can be useful as epitopes in any of the various embodiments of the invention. Any of SEQ ID NOS. 603-610 can be useful as sequences containing epitopes or epitope clusters, as described in various embodiments of the invention.

5 **All accession numbers used here and throughout can be accessed through the NCBI databases, for example, through the Entrez seek and retrieval system on the world wide web.

10 Note that the following discussion sets forth the inventors' understanding of the operation of the invention. However, it is not intended that this discussion limit the patent to any particular theory of operation not set forth in the claims.

15 In pursuing the development of epitope vaccines others have generated lists of predicted epitopes based on MHC binding motifs. Such peptides can be immunogenic, but may not correspond to any naturally produced antigenic fragment. Therefore, whole antigen will not elicit a similar response or sensitize a target cell to cytolysis by CTL. Therefore such lists do not
20 differentiate between those sequences that can be useful as vaccines and those that cannot. Efforts to determine which of these predicted epitopes are in fact naturally produced have often relied on screening their reactivity with tumor infiltrating lymphocytes (TIL). However, TIL are strongly biased to recognize immune epitopes whereas tumors (and chronically infected cells) will generally present housekeeping epitopes. Thus, unless the epitope is produced by both the housekeeping and
25 immuno- proteasomes, the target cell will generally not be recognized by CTL induced with TIL-identified epitopes. The epitopes of the present invention, in contrast, are generated by the action of a specified proteasome, indicating that they can be naturally produced, and enabling their appropriate use. The importance of the distinction between housekeeping and immune epitopes to vaccine design is more fully set forth in PCT publication WO 01/82963A2. The teachings and
embodiments disclosed in said PCT publication are contemplated as supporting principals and
embodiments related to and useful in connection with the present invention.

30 The epitopes of the invention include or encode polypeptide fragments of TAAs that are precursors or products of proteasomal cleavage by a housekeeping or immune proteasome, and that contain or consist of a sequence having a known or predicted affinity for at least one allele of MHC
I. In some embodiments, the epitopes include or encode a polypeptide of about 6 to 25 amino acids in length, preferably about 7 to 20 amino acids in length, more preferably about 8 to 15 amino acids in length, and still more preferably 9 or 10 amino acids in length. However, it is understood that the polypeptides can be larger as long as N-terminal trimming can produce the MHC epitope or that

they do not contain sequences that cause the polypeptides to be directed away from the proteasome or to be destroyed by the proteasome. For immune epitopes, if the larger peptides do not contain such sequences, they can be processed in the pAPC by the immune proteasome. Housekeeping epitopes may also be embedded in longer sequences provided that the sequence is adapted to facilitate liberation of the epitope's C-terminus by action of the immunoproteasome. The foregoing discussion has assumed that processing of longer epitopes proceeds through action of the immunoproteasome of the pAPC. However, processing can also be accomplished through the contrivance of some other mechanism, such as providing an exogenous protease activity and a sequence adapted so that action of the protease liberates the MHC epitope. The sequences of these epitopes can be subjected to computer analysis in order to calculate physical, biochemical, immunologic, or molecular genetic properties such as mass, isoelectric point, predicted mobility in electrophoresis, predicted binding to other MHC molecules, melting temperature of nucleic acid probes, reverse translations, similarity or homology to other sequences, and the like.

In constructing the polynucleotides encoding the polypeptide epitopes of the invention, the gene sequence of the associated TAA can be used, or the polynucleotide can be assembled from any of the corresponding codons. For a 10 amino acid epitope this can constitute on the order of 10^6 different sequences, depending on the particular amino acid composition. While large, this is a distinct and readily definable set representing a miniscule fraction of the $>10^{18}$ possible polynucleotides of this length, and thus in some embodiments, equivalents of a particular sequence disclosed herein encompass such distinct and readily definable variations on the listed sequence. In choosing a particular one of these sequences to use in a vaccine, considerations such as codon usage, self-complementarity, restriction sites, chemical stability, etc. can be used as will be apparent to one skilled in the art.

The invention contemplates producing peptide epitopes. Specifically these epitopes are derived from the sequence of a TAA, and have known or predicted affinity for at least one allele of MHC I. Such epitopes are typically identical to those produced on target cells or pAPCs.

Compositions Containing Active Epitopes

Embodiments of the present invention provide polypeptide compositions, including vaccines, therapeutics, diagnostics, pharmacological and pharmaceutical compositions. The various compositions include newly identified epitopes of TAAs, as well as variants of these epitopes. Other embodiments of the invention provide polynucleotides encoding the polypeptide epitopes of the invention. The invention further provides vectors for expression of the polypeptide epitopes for purification. In addition, the invention provides vectors for the expression of the polypeptide epitopes in an APC for use as an anti-tumor vaccine. Any of the epitopes or antigens, or nucleic acids encoding the same, from Table 1 can be used. Other embodiments relate to methods of making and using the various compositions.

A general architecture for a class I MHC-binding epitope can be described, and has been reviewed more extensively in Madden, D.R. *Annu. Rev. Immunol.* 13:587-622, 1995. Much of the binding energy arises from main chain contacts between conserved residues in the MHC molecule and the N- and C-termini of the peptide. Additional main chain contacts are made but vary among MHC alleles. Sequence specificity is conferred by side chain contacts of so-called anchor residues with pockets that, again, vary among MHC alleles. Anchor residues can be divided into primary and secondary. Primary anchor positions exhibit strong preferences for relatively well-defined sets of amino acid residues. Secondary positions show weaker and/or less well-defined preferences that can often be better described in terms of less favored, rather than more favored, residues. Additionally, residues in some secondary anchor positions are not always positioned to contact the pocket on the MHC molecule at all. Thus, a subset of peptides exists that bind to a particular MHC molecule and have a side chain-pocket contact at the position in question and another subset exists that show binding to the same MHC molecule that does not depend on the conformation the peptide assumes in the peptide-binding groove of the MHC molecule. The C-terminal residue (P Ω ; omega) is preferably a primary anchor residue. For many of the better studied HLA molecules (e.g. A2, A68, B27, B7, B35, and B53) the second position (P2) is also an anchor residue. However, central anchor residues have also been observed including P3 and P5 in HLA-B8, as well as P5 and P Ω (omega)-3 in the murine MHC molecules H-2D^b and H-2K^b, respectively. Since more stable binding will generally improve immunogenicity, anchor residues are preferably conserved or optimized in the design of variants, regardless of their position.

Because the anchor residues are generally located near the ends of the epitope, the peptide can buckle upward out of the peptide-binding groove allowing some variation in length. Epitopes ranging from 8-11 amino acids have been found for HLA-A68, and up to 13 amino acids for HLA-A2. In addition to length variation between the anchor positions, single residue truncations and extensions have been reported and the N- and C-termini, respectively. Of the non-anchor residues, some point up out of the groove, making no contact with the MHC molecule but being available to contact the TCR, very often P1, P4, and P Ω (omega)-1 for HLA-A2. Others of the non-anchor residues can become interposed between the upper edges of the peptide-binding groove and the TCR, contacting both. The exact positioning of these side chain residues, and thus their effects on binding, MHC fine conformation, and ultimately immunogenicity, are highly sequence dependent. For an epitope to be highly immunogenic it must not only promote stable enough TCR binding for activation to occur, but the TCR must also have a high enough off-rate that multiple TCR molecules can interact sequentially with the same peptide-MHC complex (Kalergis, A.M. et al., *Nature Immunol.* 2:229-234, 2001). Thus, without further information about the ternary complex, both conservative and non-conservative substitutions at these positions merit consideration when designing variants.

The polypeptide epitope variants can be made, for example, using any of the techniques and guidelines for conservative and non-conservative mutations. Variants can be derived from substitution, deletion or insertion of one or more amino acids as compared with the native sequence. Amino acid substitutions can be the result of replacing one amino acid with another amino acid having similar structural and/or chemical properties, such as the replacement of a threonine with a serine, for example. Such replacements are referred to as conservative amino acid replacements, and all appropriate conservative amino acid replacements are considered to be embodiments of one invention. Insertions or deletions can optionally be in the range of about 1 to 4, preferably 1 to 2, amino acids. It is generally preferable to maintain the "anchor positions" of the peptide which are responsible for binding to the MHC molecule in question. Indeed, immunogenicity of peptides can be improved in many cases by substituting more preferred residues at the anchor positions (Franco, et al., *Nature Immunology*, 1(2):145-150, 2000). Immunogenicity of a peptide can also often be improved by substituting bulkier amino acids for small amino acids found in non-anchor positions while maintaining sufficient cross-reactivity with the original epitope to constitute a useful vaccine. The variation allowed can be determined by routine insertions, deletions or substitutions of amino acids in the sequence and testing the resulting variants for activity exhibited by the polypeptide epitope. Because the polypeptide epitope is often 9 amino acids, the substitutions preferably are made to the shortest active epitope, for example, an epitope of 9 amino acids.

Variants can also be made by adding any sequence onto the N-terminus of the polypeptide epitope variant. Such N-terminal additions can be from 1 amino acid up to at least 25 amino acids. Because peptide epitopes are often trimmed by N-terminal exopeptidases active in the pAPC, it is understood that variations in the added sequence can have no effect on the activity of the epitope. In preferred embodiments, the amino acid residues between the last upstream proteasomal cleavage site and the N-terminus of the MHC epitope do not include a proline residue. Serwold, T. et al., *Nature Immunol.* 2:644-651, 2001. Accordingly, effective epitopes can be generated from precursors larger than the preferred 9-mer class I motif.

Generally, peptides are useful to the extent that they correspond to epitopes actually displayed by MHC I on the surface of a target cell or a pACP. A single peptide can have varying affinities for different MHC molecules, binding some well, others adequately, and still others not appreciably (Table 2). MHC alleles have traditionally been grouped according to serologic reactivity which does not reflect the structure of the peptide-binding groove, which can differ among different alleles of the same type. Similarly, binding properties can be shared across types; groups based on shared binding properties have been termed supertypes. There are numerous alleles of MHC I in the human population; epitopes specific to certain alleles can be selected based on the genotype of the patient.

Table 2.

Predicted Binding of Tyrosinase₂₀₇₋₂₁₆ (SEQ ID NO. 1) to Various MHC types

| MHC I type | *Half time of dissociation (min) |
|-----------------------------------|----------------------------------|
| A1 | 0.05 |
| A*0201 | 1311. |
| A*0205 | 50.4 |
| A3 | 2.7 |
| A*1101 (part of the A3 supertype) | 0.012 |
| A24 | 6.0 |
| B7 | 4.0 |
| B8 | 8.0 |
| B14 (part of the B27 supertype) | 60.0 |
| B*2702 | 0.9 |
| B*2705 | 30.0 |
| B*3501 (part of the B7 supertype) | 2.0 |
| B*4403 | 0.1 |
| B*5101 (part of the B7 supertype) | 26.0 |
| B*5102 | 55.0 |
| B*5801 | 0.20 |
| B60 | 0.40 |
| B62 | 2.0 |

5 *HLA Peptide Binding Predictions (world wide web hypertext transfer protocol "access at bimas.dcrn.nih.gov/molbio/hla_bin").

10 In further embodiments of the invention, the epitope, as peptide or encoding polynucleotide, can be administered as a pharmaceutical composition, such as, for example, a vaccine or an immunogenic composition, alone or in combination with various adjuvants, carriers, or excipients. It should be noted that although the term vaccine may be used throughout the discussion herein, the concepts can be applied and used with any other pharmaceutical composition, including those mentioned herein. Particularly advantageous adjuvants include various cytokines and oligonucleotides containing immunostimulatory sequences (as set forth in greater detail in the co-pending applications referenced herein). Additionally the polynucleotide encoded epitope can be contained in a virus (e.g. *vaccinia* or adenovirus) or in a microbial host cell (e.g. *Salmonella* or *Listeria monocytogenes*) which is then used as a vector for the polynucleotide (Dietrich, G. et al. Nat. Biotech. 16:181-185, 1998). Alternatively a pAPC can be transformed, *ex vivo*, to express the epitope, or pulsed with peptide epitope, to be itself administered as a vaccine. To increase efficiency of these processes, the encoded epitope can be carried by a viral or bacterial vector, or complexed with a ligand of a receptor found on pAPC. Similarly the peptide epitope can be complexed with or conjugated to a pAPC ligand. A vaccine can be composed of more than a single epitope.

20 Particularly advantageous strategies for incorporating epitopes and/or epitope clusters, into a vaccine or pharmaceutical composition are disclosed in PCT Publication WO 01/82963 and U.S.

Patent Application No. 09/560,465 entitled "EPITOPE SYNCHRONIZATION IN ANTIGEN PRESENTING CELLS," filed on April 28, 2000. The teaching and embodiments disclosed in said PCT publication are contemplated as supporting principals and embodiments related to and useful in connection with the present invention. Epitope clusters for use in connection with this invention
5 are disclosed in PCT Publication WO 01/82963 and U.S. Patent Application No. 09/561,571 entitled "EPITOPE CLUSTERS," filed on April 28, 2000. The teaching and embodiments disclosed in said PCT publication are contemplated as supporting principals and embodiments related to and useful in connection with the present invention.

Preferred embodiments of the present invention are directed to vaccines and methods for
10 causing a pAPC or population of pAPCs to present housekeeping epitopes that correspond to the epitopes displayed on a particular target cell. Any of the epitopes or antigens in Table 1, can be used for example. In one embodiment, the housekeeping epitope is a TuAA epitope processed by the housekeeping proteasome of a particular tumor type. In another embodiment, the housekeeping epitope is a virus-associated epitope processed by the housekeeping proteasome of a cell infected
15 with a virus. This facilitates a specific T cell response to the target cells. Concurrent expression by the pAPCs of multiple epitopes, corresponding to different induction states (pre- and post-attack), can drive a CTL response effective against target cells as they display either housekeeping epitopes or immune epitopes.

By having both housekeeping and immune epitopes present on the pAPC, this embodiment
20 can optimize the cytotoxic T cell response to a target cell. With dual epitope expression, the pAPCs can continue to sustain a CTL response to the immune-type epitope when the tumor cell switches from the housekeeping proteasome to the immune proteasome with induction by IFN, which, for example, may be produced by tumor-infiltrating CTLs.

In a preferred embodiment, immunization of a patient is with a vaccine that includes a
25 housekeeping epitope. Many preferred TAAs are associated exclusively with a target cell, particularly in the case of infected cells. In another embodiment, many preferred TAAs are the result of deregulated gene expression in transformed cells, but are found also in tissues of the testis, ovaries and fetus. In another embodiment, useful TAAs are expressed at higher levels in the target cell than in other cells. In still other embodiments, TAAs are not differentially expressed in the
30 target cell compare to other cells, but are still useful since they are involved in a particular function of the cell and differentiate the target cell from most other peripheral cells; in such embodiments, healthy cells also displaying the TAA may be collaterally attacked by the induced T cell response, but such collateral damage is considered to be far preferable to the condition caused by the target cell.

35 The vaccine contains a housekeeping epitope in a concentration effective to cause a pAPC or populations of pAPCs to display housekeeping epitopes. Advantageously, the vaccine can

include a plurality of housekeeping epitopes or one or more housekeeping epitopes optionally in combination with one or more immune epitopes. Formulations of the vaccine contain peptides and/or nucleic acids in a concentration sufficient to cause pAPCs to present the epitopes. The formulations preferably contain epitopes in a total concentration of about 1µg-1mg/100µl of vaccine preparation. Conventional dosages and dosing for peptide vaccines and/or nucleic acid vaccines can be used with the present invention, and such dosing regimens are well understood in the art. In one embodiment, a single dosage for an adult human may advantageously be from about 1 to about 5000 µl of such a composition, administered one time or multiple times, e.g., in 2, 3, 4 or more dosages separated by 1 week, 2 weeks, 1 month, or more. insulin pump delivers 1 ul per hour (lowest frequency) ref intranodal method patent.

The compositions and methods of the invention disclosed herein further contemplate incorporating adjuvants into the formulations in order to enhance the performance of the vaccines. Specifically, the addition of adjuvants to the formulations is designed to enhance the delivery or uptake of the epitopes by the pAPCs. The adjuvants contemplated by the present invention are known by those of skill in the art and include, for example, GMCSF, GCSF, IL-2, IL-12, BCG, tetanus toxoid, osteopontin, and ETA-1.

In some embodiments of the invention, the vaccines can include a recombinant organism, such as a virus, bacterium or parasite, genetically engineered to express an epitope in a host. For example, *Listeria monocytogenes*, a gram-positive, facultative intracellular bacterium, is a potent vector for targeting TuAAs to the immune system. In a preferred embodiment, this vector can be engineered to express a housekeeping epitope to induce therapeutic responses. The normal route of infection of this organism is through the gut and can be delivered orally. In another embodiment, an adenovirus (Ad) vector encoding a housekeeping epitope for a TuAA can be used to induce anti-virus or anti-tumor responses. Bone marrow-derived dendritic cells can be transduced with the virus construct and then injected, or the virus can be delivered directly via subcutaneous injection into an animal to induce potent T-cell responses. Another embodiment employs a recombinant vaccinia virus engineered to encode amino acid sequences corresponding to a housekeeping epitope for a TAA. Vaccinia viruses carrying constructs with the appropriate nucleotide substitutions in the form of a minigene construct can direct the expression of a housekeeping epitope, leading to a therapeutic T cell response against the epitope.

The immunization with DNA requires that APCs take up the DNA and express the encoded proteins or peptides. It is possible to encode a discrete class I peptide on the DNA. By immunizing with this construct, APCs can be caused to express a housekeeping epitope, which is then displayed on class I MHC on the surface of the cell for stimulating an appropriate CTL response. Constructs generally relying on termination of translation or non-proteasomal proteases for generation of proper termini of housekeeping epitopes have been described in PCT Publication

WO 01/82963 and U.S. Patent application No. 09/561,572 entitled EXPRESSION VECTORS ENCODING EPITOPES OF TARGET-ASSOCIATED ANTIGENS, filed on April 28, 2000. The teaching and embodiments disclosed in said PCT publication are contemplated as supporting principals and embodiments related to and useful in connection with the present invention.

5 As mentioned, it can be desirable to express housekeeping peptides in the context of a larger protein. Processing can be detected even when a small number of amino acids are present beyond the terminus of an epitope. Small peptide hormones are usually proteolytically processed from longer translation products, often in the size range of approximately 60-120 amino acids. This fact has led some to assume that this is the minimum size that can be efficiently translated. In
10 some embodiments, the housekeeping peptide can be embedded in a translation product of at least about 60 amino acids. In other embodiments the housekeeping peptide can be embedded in a translation product of at least about 50, 30, or 15 amino acids.

Due to differential proteasomal processing, the immune proteasome of the pAPC produces peptides that are different from those produced by the housekeeping proteasome in peripheral body
15 cells. Thus, in expressing a housekeeping peptide in the context of a larger protein, it is preferably expressed in the APC in a context other than its full length native sequence, because, as a housekeeping epitope, it is generally only efficiently processed from the native protein by the housekeeping proteasome, which is not active in the APC. In order to encode the housekeeping epitope in a DNA sequence encoding a larger protein, it is useful to find flanking areas on either
20 side of the sequence encoding the epitope that permit appropriate cleavage by the immune proteasome in order to liberate that housekeeping epitope. Altering flanking amino acid residues at the N-terminus and C-terminus of the desired housekeeping epitope can facilitate appropriate cleavage and generation of the housekeeping epitope in the APC. Sequences embedding housekeeping epitopes can be designed *de novo* and screened to determine which can be
25 successfully processed by immune proteasomes to liberate housekeeping epitopes.

Alternatively, another strategy is very effective for identifying sequences allowing production of housekeeping epitopes in APC. A contiguous sequence of amino acids can be generated from head to tail arrangement of one or more housekeeping epitopes. A construct expressing this sequence is used to immunize an animal, and the resulting T cell response is
30 evaluated to determine its specificity to one or more of the epitopes in the array. By definition, these immune responses indicate housekeeping epitopes that are processed in the pAPC effectively. The necessary flanking areas around this epitope are thereby defined. The use of flanking regions of about 4-6 amino acids on either side of the desired peptide can provide the necessary information to facilitate proteasome processing of the housekeeping epitope by the immune
35 proteasome. Therefore, a sequence ensuring epitope synchronization of approximately 16-22 amino acids can be inserted into, or fused to, any protein sequence effectively to result in that

housekeeping epitope being produced in an APC. In alternate embodiments the whole head-to-tail array of epitopes, or just the epitopes immediately adjacent to the correctly processed housekeeping epitope can be similarly transferred from a test construct to a vaccine vector.

In a preferred embodiment, the housekeeping epitopes can be embedded between known
5 immune epitopes, or segments of such, thereby providing an appropriate context for processing. The abutment of housekeeping and immune epitopes can generate the necessary context to enable the immune proteasome to liberate the housekeeping epitope, or a larger fragment, preferably including a correct C-terminus. It can be useful to screen constructs to verify that the desired epitope is produced. The abutment of housekeeping epitopes can generate a site cleavable by the
10 immune proteasome. Some embodiments of the invention employ known epitopes to flank housekeeping epitopes in test substrates; in others, screening as described below are used whether the flanking regions are arbitrary sequences or mutants of the natural flanking sequence, and whether or not knowledge of proteasomal cleavage preferences are used in designing the substrates.

15 Cleavage at the mature N-terminus of the epitope, while advantageous, is not required, since a variety of N-terminal trimming activities exist in the cell that can generate the mature N-terminus of the epitope subsequent to proteasomal processing. It is preferred that such N-terminal extension be less than about 25 amino acids in length and it is further preferred that the extension have few or no proline residues. Preferably, in screening, consideration is given not only to
20 cleavage at the ends of the epitope (or at least at its C-terminus), but consideration also can be given to ensure limited cleavage within the epitope.

Shotgun approaches can be used in designing test substrates and can increase the efficiency of screening. In one embodiment multiple epitopes can be assembled one after the other, with individual epitopes possibly appearing more than once. The substrate can be screened to determine
25 which epitopes can be produced. In the case where a particular epitope is of concern a substrate can be designed in which it appears in multiple different contexts. When a single epitope appearing in more than one context is liberated from the substrate additional secondary test substrates, in which individual instances of the epitope are removed, disabled, or are unique, can be used to determine which are being liberated and truly constitute sequences ensuring epitope synchronization.

30 Several readily practicable screens exist. A preferred *in vitro* screen utilizes proteasomal digestion analysis, using purified immune proteasomes, to determine if the desired housekeeping epitope can be liberated from a synthetic peptide embodying the sequence in question. The position of the cleavages obtained can be determined by techniques such as mass spectrometry, HPLC, and N-terminal pool sequencing; as described in greater detail in U. S. Patent Applications entitled
35 METHOD OF EPITOPE DISCOVERY, EPITOPE SYNCHRONIZATION IN ANTIGEN

PRESENTING CELLS, PCT Publication, U.S. applications and Provisional U. S. Patent Applications entitled EPITOPE SEQUENCES.

Alternatively, *in vivo* screens such as immunization or target sensitization can be employed. For immunization a nucleic acid construct capable of expressing the sequence in question is used. Harvested CTL can be tested for their ability to recognize target cells presenting the housekeeping epitope in question. Such targets cells are most readily obtained by pulsing cells expressing the appropriate MHC molecule with synthetic peptide embodying the mature housekeeping epitope. Alternatively, cells known to express housekeeping proteasome and the antigen from which the housekeeping epitope is derived, either endogenously or through genetic engineering, can be used. To use target sensitization as a screen, CTL, or preferably a CTL clone, that recognizes the housekeeping epitope can be used. In this case it is the target cell that expresses the embedded housekeeping epitope (instead of the pAPC during immunization) and it must express immune proteasome. Generally, the target cell can be transformed with an appropriate nucleic acid construct to confer expression of the embedded housekeeping epitope. Loading with a synthetic peptide embodying the embedded epitope using peptide loaded liposomes or a protein transfer reagent such as BIOPORTER™ (Gene Therapy Systems, San Diego, CA) represents an alternative.

Additional guidance on nucleic acid constructs useful as vaccines in accordance with the present invention are disclosed in WO 01/82963 and U.S. Patent Application No. 09/561,572 entitled "EXPRESSION VECTORS ENCODING EPITOPES OF TARGET-ASSOCIATED ANTIGENS," filed on April 28, 2000. Further, expression vectors and methods for their design, which are useful in accordance with the present invention are disclosed in PCT Publication WO 03/063770; U.S. Patent Application No. 10/292,413, filed on November 7, 2002; and U.S. Provisional Application No. 60/336,968 (attorney docket number CTLIMM.022PR) entitled "EXPRESSION VECTORS ENCODING EPITOPES OF TARGET-ASSOCIATED ANTIGENS AND METHODS FOR THEIR DESIGN," filed on 11/7/2001. The teaching and embodiments disclosed in said PCT publications are contemplated as supporting principals and embodiments related to and useful in connection with the present invention.

A preferred embodiment of the present invention includes a method of administering a vaccine including an epitope (or epitopes) to induce a therapeutic immune response. The vaccine is administered to a patient in a manner consistent with the standard vaccine delivery protocols that are known in the art. Methods of administering epitopes of TAAs including, without limitation, transdermal, intranodal, perinodal, oral, intravenous, intradermal, intramuscular, intraperitoneal, and mucosal administration, including delivery by injection, instillation or inhalation. A particularly useful method of vaccine delivery to elicit a CTL response is disclosed in Australian Patent No. 739189 issued January 17, 2002; PCT Publication No. WO 099/02183; U.S. Patent

Application No. 09/380,534, filed on September 1, 1999; a Continuation-in-Part thereof U.S. Patent Application No. 09/776,232 both entitled "A METHOD OF INDUCING A CTL RESPONSE," filed on February 2, 2001, published as 20020007173; and PCT Publication No. WO 02/062368. The teachings and embodiments disclosed in said publications and applications are contemplated as supporting principals and embodiments related to and useful in connection with the present invention.

Reagents Recognizing Epitopes

In another aspect of the invention, proteins with binding specificity for the epitope and/or the epitope-MHC molecule complex are contemplated, as well as the isolated cells by which they can be expressed. In one set of embodiments these reagents take the form of immunoglobulins: polyclonal sera or monoclonal antibodies (mAb), methods for the generation of which are well known in the art. Generation of mAb with specificity for peptide-MHC molecule complexes is known in the art. See, for example, Aharoni et al. *Nature* 351:147-150, 1991; Andersen et al. *Proc. Natl. Acad. Sci. USA* 93:1820-1824, 1996; Dadaglio et al. *Immunity* 6:727-738, 1997; Duc et al. *Int. Immunol.* 5:427-431, 1993; Eastman et al. *Eur. J. Immunol.* 26:385-393, 1996; Engberg et al. *Immunotechnology* 4:273-278, 1999; Porgdor et al. *Immunity* 6:715-726, 1997; Puri et al. *J. Immunol.* 158:2471-2476, 1997; and Polakova, K., et al. *J. Immunol.* 165 342-348, 2000.

In other embodiments the compositions can be used to induce and generate, *in vivo* and *in vitro*, T-cells specific for the any of the epitopes and/or epitope-MHC complexes. In preferred embodiments the epitope can be any one or more of those listed in TABLE 1, for example. Thus, embodiments also relate to and include isolated T cells, T cell clones, T cell hybridomas, or a protein containing the T cell receptor (TCR) binding domain derived from the cloned gene, as well as a recombinant cell expressing such a protein. Such TCR derived proteins can be simply the extra-cellular domains of the TCR, or a fusion with portions of another protein to confer a desired property or function. One example of such a fusion is the attachment of TCR binding domains to the constant regions of an antibody molecule so as to create a divalent molecule. The construction and activity of molecules following this general pattern have been reported, for example, Plaksin, D. et al. *J. Immunol.* 158:2218-2227, 1997 and Lebowitz, M.S. et al. *Cell Immunol.* 192:175-184, 1999. The more general construction and use of such molecules is also treated in U.S. patent 5,830,755 entitled T CELL RECEPTORS AND THEIR USE IN THERAPEUTIC AND DIAGNOSTIC METHODS.

The generation of such T cells can be readily accomplished by standard immunization of laboratory animals, and reactivity to human target cells can be obtained by immunizing with human target cells or by immunizing HLA-transgenic animals with the antigen/epitope. For some therapeutic approaches T cells derived from the same species are desirable. While such a cell can be created by cloning, for example, a murine TCR into a human T cell as contemplated above, *in*

vitro immunization of human cells offers a potentially faster option. Techniques for *in vitro* immunization, even using naive donors, are known in the field, for example, Stauss et al., *Proc. Natl. Acad. Sci. USA* 89:7871-7875, 1992; Salgaller et al. *Cancer Res.* 55:4972-4979, 1995; Tsai et al., *J. Immunol.* 158:1796-1802, 1997; and Chung et al., *J. Immunother.* 22:279-287, 1999.

5 Any of these molecules can be conjugated to enzymes, radiochemicals, fluorescent tags, and toxins, so as to be used in the diagnosis (imaging or other detection), monitoring, and treatment of the pathogenic condition associated with the epitope. Thus a toxin conjugate can be administered to kill tumor cells, radiolabeling can facilitate imaging of epitope positive tumor, an enzyme conjugate can be used in an ELISA-like assay to diagnose cancer and confirm epitope
10 expression in biopsied tissue. In a further embodiment, such T cells as set forth above, following expansion accomplished through stimulation with the epitope and/or cytokines, can be administered to a patient as an adoptive immunotherapy.

Reagents Comprising Epitopes

A further aspect of the invention provides isolated epitope-MHC complexes. In a
15 particularly advantageous embodiment of this aspect of the invention, the complexes can be soluble, multimeric proteins such as those described in U. S. Patent No. 5,635,363 (tetramers) or U. S. Patent No. 6,015,884 (Ig-dimers). Such reagents are useful in detecting and monitoring specific T cell responses, and in purifying such T cells.

Isolated MHC molecules complexed with epitopic peptides can also be incorporated into
20 planar lipid bilayers or liposomes. Such compositions can be used to stimulate T cells *in vitro* or, in the case of liposomes, *in vivo*. Co-stimulatory molecules (e.g. B7, CD40, LFA-3) can be incorporated into the same compositions or, especially for *in vitro* work, co-stimulation can be provided by anti-co-receptor antibodies (e.g. anti-CD28, anti-CD154, anti-CD2) or cytokines (e.g. IL-2, IL-12). Such stimulation of T cells can constitute vaccination, drive expansion of T cells
25 *in vitro* for subsequent infusion in an immunotherapy, or constitute a step in an assay of T cell function.

The epitope, or more directly its complex with an MHC molecule, can be an important constituent of functional assays of antigen-specific T cells at either an activation or readout step or both. Of the many assays of T cell function current in the art (detailed procedures can be found in
30 standard immunological references such as *Current Protocols in Immunology* 1999 John Wiley & Sons Inc., N.Y.) two broad classes can be defined, those that measure the response of a pool of cells and those that measure the response of individual cells. Whereas the former conveys a global measure of the strength of a response, the latter allows determination of the relative frequency of responding cells. Examples of assays measuring global response are cytotoxicity assays, ELISA,
35 and proliferation assays detecting cytokine secretion. Assays measuring the responses of individual cells (or small clones derived from them) include limiting dilution analysis (LDA),

ELISPOT, flow cytometric detection of unsecreted cytokine (described in U.S. Patent No. 5,445,939, entitled "METHOD FOR ASSESSMENT OF THE MONONUCLEAR LEUKOCYTE IMMUNE SYSTEM" and U.S. Patent Nos 5,656,446; and 5,843,689, both entitled "METHOD FOR THE ASSESSMENT OF THE MONONUCLEAR LEUKOCYTE IMMUNE SYSTEM,"
5 reagents for which are sold by Becton, Dickinson & Company under the tradename 'FASTIMMUNE') and detection of specific TCR with tetramers or Ig-dimers as stated and referenced above. The comparative virtues of these techniques have been reviewed in Yee, C. et al. *Current Opinion in Immunology*, 13:141-146, 2001. Additionally detection of a specific TCR rearrangement or expression can be accomplished through a variety of established nucleic acid
10 based techniques, particularly in situ and single-cell PCR techniques, as will be apparent to one of skill in the art.

These functional assays are used to assess endogenous levels of immunity, response to an immunologic stimulus (e.g. a vaccine), and to monitor immune status through the course of a disease and treatment. Except when measuring endogenous levels of immunity, any of these assays
15 presume a preliminary step of immunization, whether *in vivo* or *in vitro* depending on the nature of the issue being addressed. Such immunization can be carried out with the various embodiments of the invention described above or with other forms of immunogen (e.g., pAPC-tumor cell fusions) that can provoke similar immunity. With the exception of PCR and tetramer/Ig-dimer type analyses which can detect expression of the cognate TCR, these assays generally benefit from a
20 step of *in vitro* antigenic stimulation which can advantageously use various embodiments of the invention as described above in order to detect the particular functional activity (highly cytolytic responses can sometimes be detected directly). Finally, detection of cytolytic activity requires epitope-displaying target cells, which can be generated using various embodiments of the invention. The particular embodiment chosen for any particular step depends on the question to be
25 addressed, ease of use, cost, and the like, but the advantages of one embodiment over another for any particular set of circumstances will be apparent to one of skill in the art.

The peptide MHC complexes described in this section have traditionally been understood to be non-covalent associations. However it is possible, and can be advantageous, to create a covalent linkages, for example by encoding the epitope and MHC heavy chain or the epitope, β 2-microglobulin, and MHC heavy chain as a single protein (Yu, Y.L.Y., et al., *J. Immunol.* 168:3145-3149, 2002; Mottez, E., et al., *J. Exp. Med.* 181:493,1995; Dela Cruz, C. S., et al., *Int. Immunol.* 12:1293, 2000; Mage, M. G., et al., *Proc. Natl. Acad. Sci. USA* 89:10658,1992; Toshitani, K., et al., *Proc. Natl. Acad. Sci. USA* 93:236,1996; Lee, L., et al., *Eur. J. Immunol.* 24:2633,1994; Chung, D. H., et al., *J. Immunol.* 163:3699,1999; Uger, R. A. and B. H. Barber, *J. Immunol.* 160:1598,
30 1998; Uger, R. A., et al., *J. Immunol.* 162:6024,1999; and White, J., et al., *J. Immunol.* 162:2671, 1999). Such constructs can have superior stability and overcome roadblocks in the processing-

presentation pathway. They can be used in the already described vaccines, reagents, and assays in similar fashion.

Tumor Associated Antigens

Epitopes of the present invention are derived from the TuAAs tyrosinase (SEQ ID NO. 2),
5 SSX-2, (SEQ ID NO. 3), PSMA (prostate-specific membrane antigen) (SEQ ID NO. 4), MAGE-1
(SEQ ID NO. 71), MAGE-2 (SEQ ID NO. 72), MAGE-3 (SEQ ID NO. 73), PRAME, (SEQ ID NO.
77), PSA, (SEQ ID NO. 78), PSCA, (SEQ ID NO. 79), CEA (carcinoembryonic antigen), (SEQ ID
NO. 88), SCP-1 (SEQ ID NO. 92), GAGE-1, (SEQ ID NO. 96), survivin, (SEQ ID NO. 98), Melan-
A/MART-1 (SEQ ID NO. 100), and BAGE (SEQ ID NO. 102). The natural coding sequences for
10 these fifteen proteins, or any segments within them, can be determined from their cDNA or
complete coding (cgs) sequences, SEQ ID NOS. 5-7, 81-83, 85-87, 89, 93, 97, 99, 101, and 103,
respectively.

Tyrosinase is a melanin biosynthetic enzyme that is considered one of the most specific
markers of melanocytic differentiation. Tyrosinase is expressed in few cell types, primarily in
15 melanocytes, and high levels are often found in melanomas. The usefulness of tyrosinase as a
TuAA is taught in U.S. Patent 5,747,271 entitled "METHOD FOR IDENTIFYING INDIVIDUALS
SUFFERING FROM A CELLULAR ABNORMALITY SOME OF WHOSE ABNORMAL
CELLS PRESENT COMPLEXES OF HLA-A2/TYROSINASE DERIVED PEPTIDES, AND
METHODS FOR TREATING SAID INDIVIDUALS."

20 GP100, also known as PMel17, also is a melanin biosynthetic protein expressed at high
levels in melanomas. GP100 as a TuAA is disclosed in U.S. Patent 5,844,075 entitled
"MELANOMA ANTIGENS AND THEIR USE IN DIAGNOSTIC AND THERAPEUTIC
METHODS."

Melan-A, also called MART-1 (Melanoma Antigen Recognized by T cells), is another
25 melanin biosynthetic protein expressed at high levels in melanomas. The usefulness of Melan-
A/MART-1 as a TuAA is taught in U.S. Patent Nos. 5,874,560 and 5,994,523 both entitled
"MELANOMA ANTIGENS AND THEIR USE IN DIAGNOSTIC AND THERAPEUTIC
METHODS," as well as U.S. Patent No. 5,620,886, entitled "ISOLATED NUCLEIC ACID
SEQUENCE CODING FOR A TUMOR REJECTION ANTIGEN PRECURSOR PROCESSED
30 TO AT LEAST ONE TUMOR REJECTION ANTIGEN PRESENTED BY HLA-A2."

SSX-2, also know as Hom-Mel-40, is a member of a family of highly conserved cancer-
testis antigens (Gure, A.O. et al. *Int. J. Cancer* 72:965-971, 1997). Its identification as a TuAA is
taught in U.S. Patent 6,025,191 entitled "ISOLATED NUCLEIC ACID MOLECULES WHICH
ENCODE A MELANOMA SPECIFIC ANTIGEN AND USES THEREOF." Cancer-testis
35 antigens are found in a variety of tumors, but are generally absent from normal adult tissues except
testis. Expression of different members of the SSX family have been found variously in tumor cell

lines. Due to the high degree of sequence identity among SSX family members, similar epitopes from more than one member of the family will be generated and able to bind to an MHC molecule, so that some vaccines directed against one member of this family can cross-react and be effective against other members of this family (see example 3 below).

5 MAGE-1, MAGE-2, and MAGE-3 are members of another family of cancer-testis antigens originally discovered in melanoma (MAGE is a contraction of melanoma-associated antigen) but found in a variety of tumors. The identification of MAGE proteins as TuAAs is taught in U.S. Patent 5,342,774 entitled NUCLEOTIDE SEQUENCE ENCODING THE TUMOR REJECTION ANTIGEN PRECURSOR, MAGE-1, and in numerous subsequent patents. Currently there are 17
10 entries for (human) MAGE in the SWISS Protein database. There is extensive similarity among these proteins so in many cases, an epitope from one can induce a cross-reactive response to other members of the family. A few of these have not been observed in tumors, most notably MAGE-H1 and MAGE-D1, which are expressed in testes and brain, and bone marrow stromal cells, respectively. The possibility of cross-reactivity on normal tissue is ameliorated by the fact that they
15 are among the least similar to the other MAGE proteins.

 GAGE-1 is a member of the GAGE family of cancer testis antigens (Van den Eynde, B., et al., *J. Exp. Med.* 182: 689-698, 1995; U.S Patent Nos. 5,610,013; 5,648,226; 5,858,689; 6,013,481; and 6,069,001). The PubGene database currently lists 12 distinct accessible members, some of which are synonymously known as PAGE or XAGE. GAGE-1 through GAGE-8 have a very high
20 degree of sequence identity, so most epitopes can be shared among multiple members of the family.

 BAGE is a cancer-testis antigen commonly expressed in melanoma, particularly metastatic melanoma, as well as in carcinomas of the lung, breast, bladder, and squamous cells of the head and neck. It's usefulness as a TuAA is taught in U.S. Patent Nos. 5,683,88 entitled "TUMOR REJECTION ANTIGENS WHICH CORRESPOND TO AMINO ACID SEQUENCES IN TUMOR
25 REJECTION ANTIGEN PRECURSOR BAGE, AND USES THEREOF" and 5,571,711 entitled "ISOLATED NUCLEIC ACID MOLECULES CODING FOR BAGE TUMOR REJECTION ANTIGEN PRECURSORS."

 NY-ESO-1, is a cancer-testis antigen found in a wide variety of tumors, also known as CTAG-1 (Cancer-Testis Antigen-1) and CAG-3 (Cancer Antigen-3). NY-ESO-1 as a TuAA is
30 disclosed in U.S. Patent 5,804,381 entitled ISOLATED NUCLEIC ACID MOLECULE ENCODING AN ESOPHAGEAL CANCER ASSOCIATED ANTIGEN, THE ANTIGEN ITSELF, AND USES THEREOF. A paralogous locus encoding antigens with extensive sequence identity, LAGE-1a/s (SEQ ID NO. 75) and LAGE-1b/L (SEQ ID NO. 76), have been disclosed in publicly available assemblies of the human genome, and have been concluded to arise through alternate
35 splicing. Additionally, CT-2 (or CTAG-2, Cancer-Testis Antigen-2) appears to be either an allele, a mutant, or a sequencing discrepancy of LAGE-1b/L. Due to the extensive sequence identity,

many epitopes from NY-ESO-1 can also induce immunity to tumors expressing these other antigens. See figure 1. The proteins are virtually identical through amino acid 70. From 71-134 the longest run of identities between NY-ESO-1 and LAGE is 6 residues, but potentially cross-reactive sequences are present. And from 135-180 NY-ESO and LAGE-1a/s are identical except
5 for a single residue, but LAGE-1b/L is unrelated due to the alternate splice. The CAMEL and LAGE-2 antigens appear to derive from the LAGE-1 mRNA, but from alternate reading frames, thus giving rise to unrelated protein sequences. More recently, GenBank Accession AF277315.5, Homo sapiens chromosome X clone RP5-865E18, RP5-1087L19, complete sequence, reports three independent loci in this region which are labeled as LAGE1 (corresponding to CTAG-2 in the
10 genome assemblies), plus LAGE2-A and LAGE2-B (both corresponding to CTAG-1 in the genome assemblies).

PSMA (prostate-specific membranes antigen), a TuAA described in U.S. Patent 5,538,866 entitled "PROSTATE-SPECIFIC MEMBRANES ANTIGEN", is expressed by normal prostate epithelium and, at a higher level, in prostatic cancer. It has also been found in the neovasculature
15 of non-prostatic tumors. PSMA can thus form the basis for vaccines directed to both prostate cancer and to the neovasculature of other tumors. This later concept is more fully described in U.S. Patent Publication No. 20030046714; PCT Publication No. WO 02/069907; and a provisional U.S. Patent application No. 60/274,063 entitled ANTI-NEOVASCULAR VACCINES FOR CANCER, filed March 7, 2001, and U.S. Application No. 10/094,699, attorney docket number
20 CTLIMM.015A, filed on March 7, 2002, entitled "ANTI-NEOVASCULAR PREPARATIONS FOR CANCER." The teachings and embodiments disclosed in said publications and applications are contemplated as supporting principals and embodiments related to and useful in connection with the present invention. Briefly, as tumors grow they recruit ingrowth of new blood vessels. This is understood to be necessary to sustain growth as the centers of unvascularized tumors are
25 generally necrotic and angiogenesis inhibitors have been reported to cause tumor regression. Such new blood vessels, or neovasculature, express antigens not found in established vessels, and thus can be specifically targeted. By inducing CTL against neovascular antigens the vessels can be disrupted, interrupting the flow of nutrients to (and removal of wastes from) tumors, leading to regression.

30 Alternate splicing of the PSMA mRNA also leads to a protein with an apparent start at Met₅₈, thereby deleting the putative membrane anchor region of PSMA as described in U.S. Patent 5,935,818 entitled "ISOLATED NUCLEIC ACID MOLECULE ENCODING ALTERNATIVELY SPLICED PROSTATE-SPECIFIC MEMBRANES ANTIGEN AND USES THEREOF." A protein termed PSMA-like protein, Genbank accession number AF261715, is nearly identical to amino
35 acids 309-750 of PSMA and has a different expression profile. Thus the most preferred epitopes are those with an N-terminus located from amino acid 58 to 308.

PRAME, also known as MAPE, DAGE, and OIP4, was originally observed as a melanoma antigen. Subsequently, it has been recognized as a CT antigen, but unlike many CT antigens (e.g., MAGE, GAGE, and BAGE) it is expressed in acute myeloid leukemias. PRAME is a member of the MAPE family which consists largely of hypothetical proteins with which it shares limited
5 sequence similarity. The usefulness of PRAME as a TuAA is taught in U.S. Patent 5,830,753 entitled "ISOLATED NUCLEIC ACID MOLECULES CODING FOR TUMOR REJECTION ANTIGEN PRECURSOR DAGE AND USES THEREOF."

PSA, prostate specific antigen, is a peptidase of the kallikrein family and a differentiation antigen of the prostate. Expression in breast tissue has also been reported. Alternate names include
10 gamma-seminoprotein, kallikrein 3, seminogelase, seminin, and P-30 antigen. PSA has a high degree of sequence identity with the various alternate splicing products prostatic/glandular kallikrein-1 and -2, as well as kallikrein 4, which is also expressed in prostate and breast tissue. Other kallikreins generally share less sequence identity and have different expression profiles. Nonetheless, cross-reactivity that might be provoked by any particular epitope, along with the
15 likelihood that that epitope would be liberated by processing in non-target tissues (most generally by the housekeeping proteasome), should be considered in designing a vaccine.

PSCA, prostate stem cell antigen, and also known as SCAH-2, is a differentiation antigen preferentially expressed in prostate epithelial cells, and overexpressed in prostate cancers. Lower level expression is seen in some normal tissues including neuroendocrine cells of the digestive tract
20 and collecting ducts of the kidney. PSCA is described in U.S. Patent 5,856,136 entitled "HUMAN STEM CELL ANTIGENS."

Synaptonemal complex protein 1 (SCP-1), also known as HOM-TES-14, is a meiosis-associated protein and also a cancer-testis antigen (Tureci, O., et al. *Proc. Natl. Acad. Sci. USA* 95:5211-5216, 1998). As a cancer antigen its expression is not cell-cycle regulated and it is found
25 frequently in gliomas, breast, renal cell, and ovarian carcinomas. It has some similarity to myosins, but with few enough identities that cross-reactive epitopes are not an immediate prospect.

The ED-B domain of fibronectin is also a potential target. Fibronectin is subject to developmentally regulated alternative splicing, with the ED-B domain being encoded by a single exon that is used primarily in oncofetal tissues (Matsuura, H. and S. Hakomori *Proc. Natl. Acad. Sci. USA* 82:6517-6521, 1985; Carnemolla, B. et al. *J. Cell Biol.* 108:1139-1148, 1989; Loridon-
30 Rosa, B. et al. *Cancer Res.* 50:1608-1612, 1990; Nicolo, G. et al. *Cell Differ. Dev.* 32:401-408, 1990; Borsi, L. et al. *Exp. Cell Res.* 199:98-105, 1992; Oyama, F. et al. *Cancer Res.* 53:2005-2011, 1993; Mandel, U. et al. *APMIS* 102:695-702, 1994; Farnoud, M.R. et al. *Int. J. Cancer* 61:27-34, 1995; Pujuguet, P. et al. *Am. J. Pathol.* 148:579-592, 1996; Gabler, U. et al. *Heart* 75:358-362, 1996; Chevalier, X. *Br. J. Rheumatol.* 35:407-415, 1996; Midulla, M. *Cancer Res.* 60:164-169, 2000).

The ED-B domain is also expressed in fibronectin of the neovasculature (Kaczmarek, J. et al. *Int. J. Cancer* 59:11-16, 1994; Castellani, P. et al. *Int. J. Cancer* 59:612-618, 1994; Neri, D. et al. *Nat. Biotech.* 15:1271-1275, 1997; Karelina, T.V. and A.Z. Eisen *Cancer Detect. Prev.* 22:438-444, 1998; Tarli, L. et al. *Blood* 94:192-198, 1999; Castellani, P. et al. *Acta Neurochir. (Wien)* 142:277-282, 2000). As an oncofetal domain, the ED-B domain is commonly found in the fibronectin expressed by neoplastic cells in addition to being expressed by the neovasculature. Thus, CTL-inducing vaccines targeting the ED-B domain can exhibit two mechanisms of action: direct lysis of tumor cells, and disruption of the tumor's blood supply through destruction of the tumor-associated neovasculature. As CTL activity can decay rapidly after withdrawal of vaccine, interference with normal angiogenesis can be minimal. The design and testing of vaccines targeted to neovasculature is described in Provisional U.S. Patent Application No. 60/274,063 entitled "ANTI-NEOVASCULATURE VACCINES FOR CANCER" and in U.S. Patent Application No. 10/094,699, attorney docket number CTLIMM.015A, entitled "ANTI-NEOVASCULATURE PREPARATIONS FOR CANCER, filed on date even with this application (March 7, 2002). A tumor cell line is disclosed in Provisional U.S. Application No. 60/363,131, filed on March 7, 2002, attorney docket number CTLIMM.028PR, entitled "HLA-TRANSGENIC MURINE TUMOR CELL LINE."

Carcinoembryonic antigen (CEA) is a paradigmatic oncofetal protein first described in 1965 (Gold and Freedman, J. *Exp. Med.* 121: 439-462, 1965. Fuller references can be found in the Online Medelian Inheritance in Man; record *114890). It has officially been renamed carcinoembryonic antigen-related cell adhesion molecule 5 (CEACAM5). Its expression is most strongly associated with adenocarcinomas of the epithelial lining of the digestive tract and in fetal colon. CEA is a member of the immunoglobulin supergene family and the defining member of the CEA subfamily.

Survivin, also known as Baculoviral IAP Repeat-Containing Protein 5 (BIRC5), is another protein with an oncofetal pattern of expression. It is a member of the inhibitor of apoptosis protein (IAP) gene family. It is widely overexpressed in cancers (Ambrosini, G. et al., *Nat. Med.* 3:917-921, 1997; Velculiscu V.E. et al., *Nat. Genet.* 23:387-388, 1999) and it's function as an inhibitor of apoptosis is believed to contribute to the malignant phenotype.

HER2/NEU is an oncogene related to the epidermal growth factor receptor (van de Vijver, et al., *New Eng. J. Med.* 319:1239-1245, 1988), and apparently identical to the c-ERBB2 oncogene (Di Fiore, et al., *Science* 237: 178-182, 1987). The over-expression of ERBB2 has been implicated in the neoplastic transformation of prostate cancer. As HER2 it is amplified and over-expressed in 25-30% of breast cancers among other tumors where expression level is correlated with the aggressiveness of the tumor (Slamon, et al., *New Eng. J. Med.* 344:783-792, 2001). A more detailed description is available in the Online Medelian Inheritance in Man; record *164870.

Useful epitopes were identified and tested as described in the following examples. However, these examples are intended for illustration purposes only, and should not be construed as limiting the scope of the invention in any way.

EXAMPLES

5 Example 1

Manufacture of epitopes.

A. Synthetic production of epitopes

Peptides having an amino acid sequence of any of SEQ ID NO: 1, 8, 9, 11-23, 26-29, 32-44, 47-54, 56-63, 66-68, or 108-602 are synthesized using either FMOC or tBOC solid phase
10 synthesis methodologies. After synthesis, the peptides are cleaved from their supports with either trifluoroacetic acid or hydrogen fluoride, respectively, in the presence of appropriate protective scavengers. After removing the acid by evaporation, the peptides are extracted with ether to remove the scavengers and the crude, precipitated peptide is then lyophilized. Purity of the crude peptides is determined by HPLC, sequence analysis, amino acid analysis, counterion content
15 analysis and other suitable means. If the crude peptides are pure enough (greater than or equal to about 90% pure), they can be used as is. If purification is required to meet drug substance specifications, the peptides are purified using one or a combination of the following: re-precipitation; reverse-phase, ion exchange, size exclusion or hydrophobic interaction chromatography; or counter-current distribution.

20 Drug product formulation

GMP-grade peptides are formulated in a parenterally acceptable aqueous, organic, or aqueous-organic buffer or solvent system in which they remain both physically and chemically stable and biologically potent. Generally, buffers or combinations of buffers or combinations of buffers and organic solvents are appropriate. The pH range is typically between 6 and 9. Organic
25 modifiers or other excipients can be added to help solubilize and stabilize the peptides. These include detergents, lipids, co-solvents, antioxidants, chelators and reducing agents. In the case of a lyophilized product, sucrose or mannitol or other lyophilization aids can be added. Peptide solutions are sterilized by membrane filtration into their final container-closure system and either lyophilized for dissolution in the clinic, or stored until use.

30 B. Construction of expression vectors for use as nucleic acid vaccines

The construction of three generic epitope expression vectors is presented below. The particular advantages of these designs are set forth in PCT Publication No. WO 01/82963 and U.S. Patent Application No. 09/561,572 entitled "EXPRESSION VECTORS ENCODING EPITOPES OF TARGET-ASSOCIATED ANTIGENS." Additional vectors strategies for their design are
35 disclosed in PCT Publication WO 03/063770; U.S. Patent Application No. 10/292,413, filed on November 7, 2002; and Provisional U.S. Patent application No. 60/336,968 entitled

“EXPRESSION VECTORS ENCODING EPITOPES OF TARGET-ASSOCIATED ANTIGENS AND METHODS FOR THEIR DESIGN,” filed on November 7, 2001. The teachings and embodiments disclosed in said PCT publications and applications are contemplated as supporting principals and embodiments related to and useful in connection with the present invention.

5 A suitable *E. coli* strain was then transfected with the plasmid and plated out onto a selective medium. Several colonies were grown up in suspension culture and positive clones were identified by restriction mapping. The positive clone was then grown up and aliquotted into storage vials and stored at -70°C.

A mini-prep (QIAprep Spin Mini-prep: Qiagen, Valencia, CA) of the plasmid was then
10 made from a sample of these cells and automated fluorescent dideoxy sequence analysis was used to confirm that the construct had the desired sequence.

B.1 Construction of pVAX-EP1-IRES-EP2

Overview:

The starting plasmid for this construct is pVAX1 purchased from Invitrogen (Carlsbad,
15 CA). Epitopes EP1 and EP2 were synthesized by GIBCO BRL (Rockville, MD). The IRES was excised from pIRES purchased from Clontech (Palo Alto, CA).

Procedure:

1. pIRES was digested with EcoRI and NotI. The digested fragments were separated by agarose gel electrophoresis, and the IRES fragment was purified from the excised
20 band.
2. pVAX1 was digested with EcoRI and NotI, and the pVAX1 fragment was gel-purified.
3. The purified pVAX1 and IRES fragments were then ligated together.
4. Competent *E. coli* of strain DH5α were transformed with the ligation mixture.
5. Minipreps were made from 4 of the resultant colonies.
- 25 6. Restriction enzyme digestion analysis was performed on the miniprep DNA. One recombinant colony having the IRES insert was used for further insertion of EP1 and EP2. This intermediate construct was called pVAX-IRES.
7. Oligonucleotides encoding EP1 and EP2 were synthesized.
8. EP1 was subcloned into pVAX-IRES between AflII and EcoRI sites, to make pVAX-EP1-IRES;
30
9. EP2 was subcloned into pVAX-EP1-IRES between SalI and NotI sites, to make the final construct pVAX-EP1-IRES-EP2.
10. The sequence of the EP1-IRES-EP2 insert was confirmed by DNA sequencing.

B 2. Construction of pVAX-EP1-IRES-EP2-ISS-NIS

Overview:

The starting plasmid for this construct was pVAX-EP1-IRES-EP2 (Example 1). The ISS (immunostimulatory sequence) introduced into this construct is AACGTT, and the NIS (standing
5 for nuclear import sequence) used is the SV40 72bp repeat sequence. ISS-NIS was synthesized by GIBCO BRL. See Figure 2.

Procedure:

1. pVAX-EP1-IRES-EP2 was digested with NruI; the linearized plasmid was gel-purified.
2. ISS-NIS oligonucleotide was synthesized.
- 10 3. The purified linearized pVAX-EP1-IRES-EP2 and synthesized ISS-NIS were ligated together.
4. Competent E. coli of strain DH5 α were transformed with the ligation product.
5. Minipreps were made from resultant colonies.
6. Restriction enzyme digestions of the minipreps were carried out.
- 15 7. The plasmid with the insert was sequenced.

B3. Construction of pVAX-EP2-UB-EP1

Overview:

The starting plasmid for this construct was pVAX1 (Invitrogen). EP2 and EP1 were synthesized by GIBCO BRL. Wild type Ubiquitin cDNA encoding the 76 amino acids in the
20 construct was cloned from yeast.

Procedure:

1. RT-PCR was performed using yeast mRNA. Primers were designed to amplify the complete coding sequence of yeast Ubiquitin.
2. The RT-PCR products were analyzed using agarose gel electrophoresis. A band with
25 the predicted size was gel-purified.
3. The purified DNA band was subcloned into pZERO1 at EcoRV site. The resulting clone was named pZERO-UB.
4. Several clones of pZERO-UB were sequenced to confirm the Ubiquitin sequence before further manipulations.
- 30 5. EP1 and EP2 were synthesized.
6. EP2, Ubiquitin and EP1 were ligated and the insert cloned into pVAX1 between BamHI and EcoRI, putting it under control of the CMV promoter.
7. The sequence of the insert EP2-UB-EP1 was confirmed by DNA sequencing.

Example 2Identification of useful epitope variants.

The 10-mer FLPWHRLFLL (SEQ ID NO. 1) is identified as a useful epitope. Based on this sequence, numerous variants are made. Variants exhibiting activity in HLA binding assays (see
5 Example 3, section 6) are identified as useful, and are subsequently incorporated into vaccines. Variants that increase the stability of binding, assayed can be particularly useful, for example as described in WO 97/41440 entitled "Methods for Selecting and Producing T Cell Peptide Epitopes and Vaccines Incorporating Said Selected Epitopes." The teachings and embodiments disclosed in said PCT publication are contemplated as supporting principals and embodiments related to and
10 useful in connection with the present invention.

The HLA-A2 binding of length variants of FLPWHRLFLL have been evaluated. Proteasomal digestion analysis indicates that the C-terminus of the 9-mer FLPWHRLFL (SEQ ID NO. 8) is also produced. Additionally the 9-mer LPWHRLFLL (SEQ ID NO. 9) can result from N-terminal trimming of the 10-mer. Both are predicted to bind to the HLA-A*0201 molecule,
15 however of these two 9-mers, FLPWHRLFL displayed more significant binding and is preferred (see Figs. 3A and B).

In vitro proteasome digestion and N-terminal pool sequencing indicates that tyrosinase₂₀₇₋₂₁₆ (SEQ ID NO. 1) is produced more commonly than tyrosinase₂₀₇₋₂₁₅ (SEQ ID NO. 8), however the latter peptide displays superior immunogenicity, a potential concern in arriving at an optimal
20 vaccine design. FLPWHRLFL, tyrosinase₂₀₇₋₂₁₅ (SEQ ID NO. 8) was used in an in vitro immunization of HLA-A2⁺ blood to generate CTL (see CTL Induction Cultures below). Using peptide pulsed T2 cells as targets in a standard chromium release assay it was found that the CTL induced by tyrosinase₂₀₇₋₂₁₅ (SEQ ID NO. 8) recognize tyrosinase₂₀₇₋₂₁₆ (SEQ ID NO. 1) targets
25 equally well (see fig. 3C). These CTL also recognize the HLA-A2⁺, tyrosinase⁺ tumor cell lines 624.38 and HTB64, but not 624.28 an HLA-A2⁻ derivative of 624.38 (fig. 3C). Thus the relative amounts of these two epitopes produced in vivo, does not become a concern in vaccine design.

CTL induction cultures

PBMCs from normal donors were purified by centrifugation in Ficoll-Hypaque from buffy coats. All cultures were carried out using the autologous plasma (AP) to avoid exposure to
30 potential xenogeneic pathogens and recognition of FBS peptides. To favor the in vitro generation of peptide-specific CTL, we employed autologous dendritic cells (DC) as APCs. DC were generated and CTL were induced with DC and peptide from PBMCs as described (Keogh et al., 2001). Briefly, monocyte-enriched cell fractions were cultured for 5 days with GM-CSF and IL-4 and were cultured for 2 additional days in culture media with 2 µg/ml CD40 ligand to induce
35 maturation. 2 x10⁶ CD8⁺-enriched T lymphocytes/well and 2 x10⁵ peptide-pulsed DC/well were co-cultured in 24-well plates in 2 ml RPMI supplemented with 10% AP, 10 ng/ml IL-7 and 20

IU/ml IL-2. Cultures were restimulated on days 7 and 14 with autologous irradiated peptide-pulsed DC.

Sequence variants of FLPWHRLFL are constructed as follow. Consistent with the binding coefficient table (see Table 3) from the NIH/BIMAS MHC binding prediction program (see reference in example 3 below), binding can be improved by changing the L at position 9, an anchor position, to V. Binding can also be altered, though generally to a lesser extent, by changes at non-anchor positions. Referring generally to Table 3, binding can be increased by employing residues with relatively larger coefficients. Changes in sequence can also alter immunogenicity independently of their effect on binding to MHC. Thus binding and/or immunogenicity can be improved as follows:

By substituting F,L,M,W, or Y for P at position 3; these are all bulkier residues that can also improve immunogenicity independent of the effect on binding. The amine and hydroxyl-bearing residues, Q and N; and S and T; respectively, can also provoke a stronger, cross-reactive response.

By substituting D or E for W at position 4 to improve binding; this addition of a negative charge can also make the epitope more immunogenic, while in some cases reducing cross-reactivity with the natural epitope. Alternatively the conservative substitutions of F or Y can provoke a cross-reactive response.

By substituting F for H at position 5 to improve binding. H can be viewed as partially charged, thus in some cases the loss of charge can hinder cross-reactivity. Substitution of the fully charged residues R or K at this position can enhance immunogenicity without disrupting charge-dependent cross-reactivity.

By substituting I, L, M, V, F, W, or Y for R at position 6. The same caveats and alternatives apply here as at position 5.

By substituting W or F for L at position 7 to improve binding. Substitution of V, I, S, T, Q, or N at this position are not generally predicted to reduce binding affinity by this model (the NIH algorithm), yet can be advantageous as discussed above.

Y and W, which are equally preferred as the Fs at positions 1 and 8, can provoke a useful cross-reactivity. Finally, while substitutions in the direction of bulkiness are generally favored to improve immunogenicity, the substitution of smaller residues such as A, S, and C, at positions 3-7 can be useful according to the theory that contrast in size, rather than bulkiness per se, is an important factor in immunogenicity. The reactivity of the thiol group in C can introduce other properties as discussed in Chen, J.-L., et al. *J. Immunol.* 165:948-955, 2000.

Table 3. 9-mer Coefficient Table for HLA-A*0201*

| HLA Coefficient table for file "A_0201_standard" | | | | | | | | | |
|--|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Amino Acid Type | 1 st | 2 nd | 3 rd | 4 th | 5 th | 6 th | 7 th | 8 th | 9 th |
| A | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 |
| C | 1.000 | 0.470 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 |
| D | 0.075 | 0.100 | 0.400 | 4.100 | 1.000 | 1.000 | 0.490 | 1.000 | 0.003 |
| E | 0.075 | 1.400 | 0.064 | 4.100 | 1.000 | 1.000 | 0.490 | 1.000 | 0.003 |
| F | 4.600 | 0.050 | 3.700 | 1.000 | 3.800 | 1.900 | 5.800 | 5.500 | 0.015 |
| G | 1.000 | 0.470 | 1.000 | 1.000 | 1.000 | 1.000 | 0.130 | 1.000 | 0.015 |
| H | 0.034 | 0.050 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 0.015 |
| I | 1.700 | 9.900 | 1.000 | 1.000 | 1.000 | 2.300 | 1.000 | 0.410 | 2.100 |
| K | 3.500 | 0.100 | 0.035 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 0.003 |
| L | 1.700 | 72.000 | 3.700 | 1.000 | 1.000 | 2.300 | 1.000 | 1.000 | 4.300 |
| M | 1.700 | 52.000 | 3.700 | 1.000 | 1.000 | 2.300 | 1.000 | 1.000 | 1.000 |
| N | 1.000 | 0.470 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 0.015 |
| P | 0.022 | 0.470 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 0.003 |
| Q | 1.000 | 7.300 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 0.003 |
| R | 1.000 | 0.010 | 0.076 | 1.000 | 1.000 | 1.000 | 0.200 | 1.000 | 0.003 |
| S | 1.000 | 0.470 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 0.015 |
| T | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.500 |
| V | 1.700 | 6.300 | 1.000 | 1.000 | 1.000 | 2.300 | 1.000 | 0.410 | 14.000 |
| W | 4.600 | 0.010 | 8.300 | 1.000 | 1.000 | 1.700 | 7.500 | 5.500 | 0.015 |
| Y | 4.600 | 0.010 | 3.200 | 1.000 | 1.000 | 1.500 | 1.000 | 5.500 | 0.015 |

*This table and other comparable data that are publicly available are useful in designing epitope variants and in determining whether a particular variant is substantially similar, or is functionally similar.

Example 3

Cluster Analysis (SSX-2₃₁₋₆₈).

1. Epitope cluster region prediction:

The computer algorithms: SYFPEITHI (internet [http:// syfpeithi.bmi-heidelberg.com/Scripts/MHCServer.dll/EpPredict.htm](http://syfpeithi.bmi-heidelberg.com/Scripts/MHCServer.dll/EpPredict.htm)), based on the book "MHC Ligands and Peptide Motifs" by H.G.Rammensee, J.Bachmann and S.Stevanovic; and HLA Peptide Binding Predictions (NIH) (internet [http:// bimas.dcrt.nih.gov/molbio/hla_bin](http://bimas.dcrt.nih.gov/molbio/hla_bin)), described in Parker, K. C., et al., *J. Immunol.* 152:163, 1994; were used to analyze the protein sequence of SSX-2 (GI:10337583). Epitope clusters (regions with higher than average density of peptide fragments with high predicted MHC affinity) were defined as described fully in U.S. Patent Application No. 09/561,571 entitled "EPITOPE CLUSTERS," filed on April 28, 2000. Using a epitope density ratio cutoff of 2, five and two clusters were defined using the SYFPETHI and NIH algorithms, respectively, and peptides score cutoffs of 16 (SYFPETHI) and 5 (NIH). The highest scoring peptide with the NIH algorithm, SSX-2₄₁₋₄₉, with an estimated halftime of dissociation of

>1000 min., does not overlap any other predicted epitope but does cluster with SSX-2₅₇₋₆₅ in the NIH analysis.

2. Peptide synthesis and characterization:

SSX-2₃₁₋₆₈, YFSKEEWEKMKASEKIFYVYMKRKYEAMTKLGFKATLP (SEQ ID NO. 10) was synthesized by MPS (Multiple Peptide Systems, San Diego, CA 92121) using standard solid phase chemistry. According to the provided 'Certificate of Analysis', the purity of this peptide was 95%.

3. Proteasome digestion:

Proteasome was isolated from human red blood cells using the proteasome isolation protocol described in PCT Publication No. WO 01/82963 and U.S. Patent Application No. 09/561,074 entitled "METHOD OF EPITOPE DISCOVERY," filed on April 28, 2000. The teachings and embodiments disclosed in said PCT publication and application are contemplated as supporting principals and embodiments related to and useful in connection with the present invention. SDS-PAGE, western-blotting, and ELISA were used as quality control assays. The final concentration of proteasome was 4 mg/ml, which was determined by non-interfering protein assay (Geno Technologies Inc.). Proteasomes were stored at -70°C in 25 µl aliquots.

SSX-2₃₁₋₆₈ was dissolved in Milli-Q water, and a 2 mM stock solution prepared and 20µL aliquots stored at -20°C.

1 tube of proteasome (25 µL) was removed from storage at -70°C and thawed on ice. It was then mixed thoroughly with 12.5µL of 2mM peptide by repipetting (samples were kept on ice). A 5µL sample was immediately removed after mixing and transferred to a tube containing 1.25µL 10%TFA (final concentration of TFA was 2%); the T=0 min sample. The proteasome digestion reaction was then started and carried out at 37°C in a programmable thermal controller. Additional 5µL samples were taken out at 15, 30, 60, 120, 180 and 240 min respectively, the reaction was stopped by adding the sample to 1.25µL 10% TFA as before. Samples were kept on ice or frozen until being analyzed by MALDI-MS. All samples were saved and stored at -20°C for HPLC analysis and N-terminal sequencing. Peptide alone (without proteasome) was used as a blank control: 2 µL peptide + 4µL Tris buffer (20 mM, pH 7.6) + 1.5µL TFA.

4. MALDI-TOF MS measurements:

For each time point 0.3 µL of matrix solution (10mg/ml α-cyano-4-hydroxycinnamic acid in AcCN/H₂O (70:30)) was first applied on a sample slide, and then an equal volume of digested sample was mixed gently with matrix solution on the slide. The slide was allowed to dry at ambient air for 3-5 min. before acquiring the mass spectra. MS was performed on a Lasermat 2000 MALDI-TOF mass spectrometer that was calibrated with peptide/protein standards. To improve the accuracy of measurement, the molecular ion weight (MH⁺) of the peptide substrate was used as

an internal calibration standard. The mass spectrum of the T=120 min. digested sample is shown in figure 4.

5. MS data analysis and epitope identification:

To assign the measured mass peaks, the computer program MS-Product, a tool from the UCSF Mass Spectrometry Facility (<http://prospector.ucsf.edu/ucsfhtml3.4/msprod.htm>), was used to generate all possible fragments (N- and C-terminal ions, and internal fragments) and their corresponding molecular weights. Due to the sensitivity of the mass spectrometer, average molecular weight was used. The mass peaks observed over the course of the digestion were identified as summarized in Table 4.

Fragments co-C-terminal with 8-10 amino acid long sequences predicted to bind HLA by the SYFPEITHI or NIH algorithms were chosen for further study. The digestion and prediction steps of the procedure can be usefully practiced in any order. Although the substrate peptide used in proteasomal digest described here was specifically designed to include predicted HLA-A2.1 binding sequences, the actual products of digestion can be checked after the fact for actual or predicted binding to other MHC molecules. Selected results are shown in Table 5.

Table 4. SSX-2₃₁₋₆₈ Mass Peak Identification.

| MS PEAK (measured) | PEPTIDE | SEQUENCE | CALCULATED MASS (MH ⁺) |
|-----------------------|---------|-------------------------------------|---------------------------------------|
| 988.23 | 31-37 | YFSKEEW | 989.08 |
| 1377.68±2.38 | 31-40 | YFSKEEWEKM | 1377.68 |
| 1662.45±1.30 | 31-43 | YFSKEEWEKMKAS | 1663.90 |
| 2181.72±0.85 | 31-47 | YFSKEEWEKMKASEKIF | 2181.52 |
| 2346.6 | 31-48 | YFSKEEWEKMKASEKIFY | 2344.71 |
| 1472.16±1.54 | 38-49 | EKMKASEKIFYV | 1473.77 |
| 2445.78±1.18 | 31-49* | YFSKEEWEKMKASEKIFYV | 2443.84 |
| 2607. | 31-50 | YFSKEEWEKMKASEKIFYVY | 2607.02 |
| 1563.3 | 50-61 | YMKRKYEAMTKL | 1562.93 |
| 3989.9 | 31-61 | YFSKEEWEKMKASEKIFYVYMKRKYEAMTKL | 3987.77 |
| 1603.74±1.53 | 51-63 | MKRKYEAMTKLGF | 1603.98 |
| 1766.45±1.5 | 50-63 | YMKRKYEAMTKLGF | 1767.16 |
| 1866.32±1.22 | 49-63 | VYMKRKYEAMTKLGF | 1866.29 |
| 4192.6 | 31-63 | YFSKEEWEKMKASEKIFYVYMKRKYEAMTKLGF | 4192.00 |
| 4392.1 | 31-65** | YFSKEEWEKMKASEKIFYVYMKRKYEAMTKLGFKA | 4391.25 |

Boldface sequence correspond to peptides predicted to bind to MHC.

* On the basis of mass alone this peak could also have been assigned to the peptide 32-50, however proteasomal removal of just the N-terminal amino acid is unlikely. N-terminal sequencing (below) verifies the assignment to 31-49.

** On the basis of mass this fragment might also represent 33-68. N-terminal sequencing below is consistent with the assignment to 31-65.

Table 5. Predicted HLA binding by proteasomally generated fragments

| SEQ ID NO. | PEPTIDE | HLA | SYFPEITHI | NIH |
|------------|---------------|--------|-----------|---------|
| 11 | FSKEEWEKM | B*3501 | NP† | 90 |
| 12 | KMKASEKIF | B*08 | 17 | <5 |
| 13 & (14) | (K) MKASEKIFY | A1 | 19 (19) | <5 |
| 15 & (16) | (M) KASEKIFYV | A*0201 | 22 (16) | 1017 |
| | | B*08 | 17 | <5 |
| | | B*5101 | 22 (13) | 60 |
| | | B*5102 | NP | 133 |
| | | B*5103 | NP | 121 |
| 17 & (18) | (K) ASEKIFYVY | A1 | 34 (19) | 14 |
| 19 & (20) | (K) RKYEAMTKL | A*0201 | 15 | <5 |
| | | A26 | 15 | NP |
| | | B14 | NP | 45 (60) |
| | | B*2705 | 21 | 15 |
| | | B*2709 | 16 | NP |
| | | B*5101 | 15 | <5 |
| 21 | KYEAMTKLGF | A1 | 16 | <5 |
| 22 | YEAMTKLGF | A24 | NP | 300 |
| 23 | EAMTKLGF | B*4403 | NP | 80 |
| | | B*08 | 22 | <5 |

†No prediction

As seen in Table 5, N-terminal addition of authentic sequence to epitopes can generate epitopes for the same or different MHC restriction elements. Note in particular the pairing of (K)RKYEAMTKL (SEQ ID NOS 19 and (20)) with HLA-B14, where the 10-mer has a longer predicted halftime of dissociation than the co-C-terminal 9-mer. Also note the case of the 10-mer KYEAMTKLGF (SEQ ID NO. 21) which can be used as a vaccine useful with several MHC types by relying on N-terminal trimming to create the epitopes for HLA-B*4403 and -B*08.

6. HLA-A0201 binding assay:

Binding of the candidate epitope KASEKIFYV, SSX-2₄₁₋₄₉, (SEQ ID NO. 15) to HLA-A2.1 was assayed using a modification of the method of Stauss et al., (Proc Natl Acad Sci USA 89(17):7871-5 (1992)). Specifically, T2 cells, which express empty or unstable MHC molecules on their surface, were washed twice with Iscove's modified Dulbecco's medium (IMDM) and cultured overnight in serum-free AIM-V medium (Life Technologies, Inc., Rockville, MD) supplemented with human β 2-microglobulin at 3 μ g/ml (Sigma, St. Louis, MO) and added peptide, at 800, 400, 200, 100, 50, 25, 12.5, and 6.25 μ g/ml in a 96-well flat-bottom plate at 3x10⁵ cells/200 μ l (microliter)/well. Peptide was mixed with the cells by repipeting before distributing to the plate (alternatively peptide can be added to individual wells), and the plate was rocked gently for 2 minutes. Incubation was in a 5% CO₂ incubator at 37°C. The next day the unbound peptide was removed by washing twice with serum free RPMI medium and a saturating amount of anti-class I HLA monoclonal antibody, fluorescein isothiocyanate (FITC)-conjugated anti-HLA A2, A28 (One

Lambda, Canoga Park, CA) was added. After incubation for 30 minutes at 4°C, cells were washed 3 times with PBS supplemented with 0.5% BSA, 0.05%(w/v) sodium azide, pH 7.4-7.6 (staining buffer). (Alternatively W6/32 (Sigma) can be used as the anti-class I HLA monoclonal antibody the cells washed with staining buffer and then incubated with fluorescein isothiocyanate (FITC)-conjugated goat F(ab') antimouse-IgG (Sigma) for 30 min at 4°C and washed 3 times as before.) The cells were resuspended in 0.5 ml staining buffer. The analysis of surface HLA-A2.1 molecules stabilized by peptide binding was performed by flow cytometry using a FACScan (Becton Dickinson, San Jose, CA). If flow cytometry is not to be performed immediately the cells can be fixed by adding a quarter volume of 2% paraformaldehyde and storing in the dark at 4°C.

The results of the experiment are shown in Figure 5. SSX-2₄₁₋₄₉ (SEQ ID NO. 15) was found to bind HLA-A2.1 to a similar extent as the known A2.1 binder FLPSDYFPSV (HBV₁₈₋₂₇; SEQ ID NO: 24) used as a positive control. An HLA-B44 binding peptide, AEMGKYSFY (SEQ ID NO: 25), was used as a negative control. The fluorescence obtained from the negative control was similar to the signal obtained when no peptide was used in the assay. Positive and negative control peptides were chosen from Table 18.3.1 in *Current Protocols in Immunology* p. 18.3.2, John Wiley and Sons, New York, 1998.

7. Immunogenicity:

A. In vivo immunization of mice.

HHD1 transgenic A*0201 mice (Pascolo, S., et al. *J. Exp. Med.* 185:2043-2051, 1997) were anesthetized and injected subcutaneously at the base of the tail, avoiding lateral tail veins, using 100 µl containing 100 nmol of SSX-2₄₁₋₄₉ (SEQ ID NO. 15) and 20 µg of HTL epitope peptide in PBS emulsified with 50 µl of IFA (incomplete Freund's adjuvant).

B. Preparation of stimulating cells (LPS blasts).

Using spleens from 2 naive mice for each group of immunized mice, un-immunized mice were sacrificed and the carcasses were placed in alcohol. Using sterile instruments, the top dermal layer of skin on the mouse's left side (lower mid-section) was cut through, exposing the peritoneum. The peritoneum was saturated with alcohol, and the spleen was aseptically extracted. The spleen was placed in a petri dish with serum-free media. Splenocytes were isolated by using sterile plungers from 3 ml syringes to mash the spleens. Cells were collected in a 50 ml conical tubes in serum-free media, rinsing dish well. Cells were centrifuged (12000 rpm, 7 min) and washed one time with RPMI. Fresh spleen cells were resuspended to a concentration of 1x10⁶ cells per ml in RPMI-10%FCS (fetal calf serum). 25g/ml lipopolysaccharide and 7 µg/ml Dextran Sulfate were added. Cell were incubated for 3 days in T-75 flasks at 37°C, with 5% CO₂. Splenic blasts were collected in 50 ml tubes pelleted (12000 rpm, 7 min) and resuspended to 3X10⁷/ml in RPMI. The blasts were pulsed with the priming peptide at 50 µg/ml, RT 4hr. mitomycin C-treated at 25µg/ml, 37°C, 20 min and washed three times with DMEM.

C. In vitro stimulation.

3 days after LPS stimulation of the blast cells and the same day as peptide loading, the primed mice were sacrificed (at 14 days post immunization) to remove spleens as above. 3×10^6 splenocytes were co-cultured with 1×10^6 LPS blasts/well in 24-well plates at 37°C , with 5% CO_2 in DMEM media supplemented with 10% FCS, 5×10^{-5} M β -mercaptoethanol, 100 $\mu\text{g/ml}$ streptomycin and 100 IU/ml penicillin. Cultures were fed 5% (vol/vol) ConA supernatant on day 3 and assayed for cytolytic activity on day 7 in a ^{51}Cr -release assay.

D. Chromium-release assay measuring CTL activity.

To assess peptide specific lysis, 2×10^6 T2 cells were incubated with 100 μCi sodium chromate together with 50 $\mu\text{g/ml}$ peptide at 37°C for 1 hour. During incubation they were gently shaken every 15 minutes. After labeling and loading, cells were washed three times with 10 ml of DMEM-10% FCS, wiping each tube with a fresh Kimwipe after pouring off the supernatant. Target cells were resuspended in DMEM-10% FBS $1 \times 10^5/\text{ml}$. Effector cells were adjusted to $1 \times 10^7/\text{ml}$ in DMEM-10% FCS and 100 μl serial 3-fold dilutions of effectors were prepared in U-bottom 96-well plates. 100 μl of target cells were added per well. In order to determine spontaneous release and maximum release, six additional wells containing 100 μl of target cells were prepared for each target. Spontaneous release was revealed by incubating the target cells with 100 μl medium; maximum release was revealed by incubating the target cells with 100 μl of 2% SDS. Plates were then centrifuged for 5 min at 600 rpm and incubated for 4 hours at 37°C in 5% CO_2 and 80% humidity. After the incubation, plates were then centrifuged for 5 min at 1200 rpm. Supernatants were harvested and counted using a gamma counter. Specific lysis was determined as follows: % specific release = $[(\text{experimental release} - \text{spontaneous release})/(\text{maximum release} - \text{spontaneous release})] \times 100$.

Results of the chromium release assay demonstrating specific lysis of peptide pulsed target cells are shown in figure 6.

8. Cross-reactivity with other SSX proteins:

SSX-2₄₁₋₄₉ (SEQ ID NO. 15) shares a high degree of sequence identity with the same region of the other SSX proteins. The surrounding regions have also been generally well conserved. Thus the housekeeping proteasome can cleave following V₄₉ in all five sequences. Moreover, SSX₄₁₋₄₉ is predicted to bind HLA-A*0201 (see Table 6). CTL generated by immunization with SSX-2₄₁₋₄₉ cross-react with tumor cells expressing other SSX proteins.

Table 6. SSX₄₁₋₄₉ – A*0201 Predicted Binding

| SEQ ID NO. | Family Member | Sequence | SYFPEITHI Score | NIH Score |
|------------|---------------|------------|-----------------|-----------|
| 15 | SSX-2 | KASEKIFYV | 22 | 1017 |
| 26 | SSX-1 | KYSEKISYV | 18 | 1.7 |
| 27 | SSX-3 | KVSEKIVYV | 24 | 1105 |
| 28 | SSX-4 | KSSEKIVYV | 20 | 82 |
| 29 | SSX-5 | KASEKIIVYV | 22 | 175 |

Example 4Cluster Analysis (PSMA₁₆₃₋₁₉₂).

- 5 [0227] A peptide, AFSPQGMPEGDLVYVNYARTEDFFKLERDM, PSMA₁₆₃₋₁₉₂, (SEQ ID NO. 30), containing an A1 epitope cluster from prostate specific membrane antigen, PSMA₁₆₈₋₁₉₀ (SEQ ID NO. 31) was synthesized using standard solid-phase F-moc chemistry on a 433A ABI Peptide synthesizer. After side chain deprotection and cleavage from the resin, peptide first dissolved in formic acid and then diluted into 30% Acetic acid, was run on a reverse-phase preparative HPLC C4 column at following conditions: linear AB gradient (5% B/min) at a flow rate of 4 ml/min, where eluent A is 0.1% aqueous TFA and eluent B is 0.1% TFA in acetonitrile. A fraction at time 16.642 min containing the expected peptide, as judged by mass spectrometry, was pooled and lyophilized. The peptide was then subjected to proteasome digestion and mass spectrum analysis essentially as described above. Prominent peaks from the mass spectra are summarized in Table 7.

Table 7. PSMA₁₆₃₋₁₉₂ Mass Peak Identification.

| PEPTIDE | SEQUENCE | CALCULATED MASS (MH ⁺) |
|---------|------------------------|------------------------------------|
| 163-177 | AFSPQGMPEGDLVYV | 1610.0 |
| 178-189 | NYARTEDFFKLE | 1533.68 |
| 170-189 | PEGDLVYVNYARTEDFFKLE | 2406.66 |
| 178-191 | NYARTEDFFKLERD | 1804.95 |
| 170-191 | PEGDLVYVNYARTEDFFKLERD | 2677.93 |
| 178-192 | NYARTEDFFKLERDM | 1936.17 |
| 163-176 | AFSPQGMPEGDLVY | 1511.70 |
| 177-192 | VNYARTEDFFKLERDM | 2035.30 |
| 163-179 | AFSPQGMPEGDLVYVNY | 1888.12 |
| 180-192 | ARTEDFFKLERDM | 1658.89 |
| 163-183 | AFSPQGMPEGDLVYVNYARTE | 2345.61 |
| 184-192 | DDFKLERDM | 1201.40 |
| 176-192 | YVNYARTEDFFKLERDM | 2198.48 |
| 167-185 | QGMPEGDLVYVNYARTEDF | 2205.41 |
| 178-186 | NYARTEDFF | 1163.22 |

Boldface sequences correspond to peptides predicted to bind to MHC, see Table 8.

N-terminal Pool Sequence Analysis

One aliquot at one hour of the proteasomal digestion (see Example 3 part 3 above) was subjected to N-terminal amino acid sequence analysis by an ABI 473A Protein Sequencer (Applied Biosystems, Foster City, CA). Determination of the sites and efficiencies of cleavage was based on consideration of the sequence cycle, the repetitive yield of the protein sequencer, and the relative yields of amino acids unique in the analyzed sequence. That is if the unique (in the analyzed sequence) residue X appears only in the nth cycle a cleavage site exists n-1 residues before it in the N-terminal direction. In addition to helping resolve any ambiguity in the assignment of mass to sequences, these data also provide a more reliable indication of the relative yield of the various fragments than does mass spectrometry.

For PSMA₁₆₃₋₁₉₂ (SEQ ID NO. 30) this pool sequencing supports a single major cleavage site after V₁₇₇ and several minor cleavage sites, particularly one after Y₁₇₉. Reviewing the results presented in figures 7A-C reveals the following:

- S at the 3rd cycle indicating presence of the N-terminus of the substrate.
- Q at the 5th cycle indicating presence of the N-terminus of the substrate.
- N at the 1st cycle indicating cleavage after V₁₇₇.
- N at the 3rd cycle indicating cleavage after V₁₇₅. Note the fragment 176-192 in Table 7.
- T at the 5th cycle indicating cleavage after V₁₇₇.
- T at the 1st–3rd cycles, indicating increasingly common cleavages after R₁₈₁, A₁₈₀ and Y₁₇₉.
- Only the last of these correspond to peaks detected by mass spectrometry; 163-179 and 180-192, see Table 7. The absence of the others can indicate that they are on fragments smaller than were examined in the mass spectrum.
- K at the 4th, 8th, and 10th cycles indicating cleavages after E₁₈₃, Y₁₇₉, and V₁₇₇, respectively, all of which correspond to fragments observed by mass spectroscopy. See Table 7.
- A at the 1st and 3rd cycles indicating presence of the N-terminus of the substrate and cleavage after V₁₇₇, respectively.
- P at the 4th and 8th cycles indicating presence of the N-terminus of the substrate.
- G at the 6th and 10th cycles indicating presence of the N-terminus of the substrate.
- M at the 7th cycle indicating presence of the N-terminus of the substrate and/or cleavage after F₁₈₅.
- M at the 15th cycle indicating cleavage after V₁₇₇.
- The 1st cycle can indicate cleavage after D₁₉₁, see Table 7.
- R at the 4th and 13th cycle indicating cleavage after V₁₇₇.
- R at the 2nd and 11th cycle indicating cleavage after Y₁₇₉.
- V at the 2nd, 6th, and 13th cycle indicating cleavage after V₁₇₅, M₁₆₉ and presence of the N-terminus of the substrate, respectively. Note fragments beginning at 176 and 170 in Table 7.

Y at the 1st, 2nd, and 14th cycles indicating cleavage after V₁₇₅, V₁₇₇, and presence of the N-terminus of the substrate, respectively.

L at the 11th and 12th cycles indicating cleavage after V₁₇₇, and presence of the N-terminus of the substrate, respectively, is the interpretation most consistent with the other data. Comparing to the mass spectrometry results we see that L at the 2nd, 5th, and 9th cycles is consistent with cleavage after F₁₈₆, E₁₈₃ or M₁₆₉, and Y₁₇₉, respectively. See Table 7.

Epitope Identification

Fragments co-C-terminal with 8-10 amino acid long sequences predicted to bind HLA by the SYFPEITHI or NIH algorithms were chosen for further analysis. The digestion and prediction steps of the procedure can be usefully practiced in any order. Although the substrate peptide used in proteasomal digest described here was specifically designed to include a predicted HLA-A1 binding sequence, the actual products of digestion can be checked after the fact for actual or predicted binding to other MHC molecules. Selected results are shown in Table 8.

Table 8. Predicted HLA binding by proteasomally generated fragments

| SEQ ID NO | PEPTIDE | HLA | SYFPEITHI | NIH |
|-----------|--------------|---------|-----------|--------|
| 32 & (33) | (G)MPEGDLVYV | A*0201 | 17 (27) | (2605) |
| | | B*0702 | 20 | <5 |
| | | B*5101 | 22 | 314 |
| 34 & (35) | (Q)GMPEGDLVY | A1 | 24 (26) | <5 |
| | | A3 | 16 (18) | 36 |
| | | B*2705 | 17 | 25 |
| | | B*5101 | 15 | NP† |
| 36 | MPEGDLVY | | | |
| 37 & (38) | (P)EGDLVYVNY | A1 | 27 (15) | 12 |
| | | A26 | 23 (17) | NP |
| 39 | LVYVNYARTE | A3 | 21 | <5 |
| 40 & (41) | (Y)VNYARTEDF | A26 | (20) | NP |
| | | B*08 | 15 | <5 |
| | | B*2705 | 12 | 50 |
| 42 | NYARTEDFF | A24 | NP† | 100 |
| | | Cw*0401 | NP | 120 |
| 43 | YARTEDFF | B*08 | 16 | <5 |
| 44 | RTEDFFKLE | A1 | 21 | <5 |
| | | A26 | 15 | NP |

†No prediction

HLA-A*0201 binding assay:

HLA-A*0201 binding studies were preformed with PSMA₁₆₈₋₁₇₇, GMPEGDLVYV, (SEQ ID NO. 33) essentially as described in Example 3 above. As seen in figure 8, this epitope exhibits significant binding at even lower concentrations than the positive control peptides. The Melan-A peptide used as a control in this assay (and throughout this disclosure), ELAGIGILTV, is actually a variant of the natural sequence (EAAGIGILTV) and exhibits a high affinity in this assay.

Example 5Cluster Analysis (PSMA₂₈₁₋₃₁₀).

Another peptide, RGIAEAVGLPSIPVHPIGYYDAQKLLEKMG, PSMA₂₈₁₋₃₁₀, (SEQ ID NO. 45), containing an A1 epitope cluster from prostate specific membrane antigen, PSMA₂₈₃₋₃₀₇ (SEQ ID NO. 46), was synthesized using standard solid-phase F-moc chemistry on a 433A ABI Peptide synthesizer. After side chain deprotection and cleavage from the resin, peptide in ddH₂O was run on a reverse-phase preparative HPLC C18 column at following conditions: linear AB gradient (5% B/min) at a flow rate of 4 ml/min, where eluent A is 0.1% aqueous TFA and eluent B is 0.1% TFA in acetonitrile. A fraction at time 17.061 min containing the expected peptide as judged by mass spectrometry, was pooled and lyophilized. The peptide was then subjected to proteasome digestion and mass spectrum analysis essentially as described above. Prominent peaks from the mass spectra are summarized in Table 9.

Table 9. PSMA₂₈₁₋₃₁₀ Mass Peak Identification.

| PEPTIDE | SEQUENCE | CALCULATE D MASS (MH ⁺) |
|---------|-----------------------------|--|
| 281-297 | RGIAEAVGLPSIPVHPI* | 1727.07 |
| 286-297 | AVGLPSIPVHPI** | 1200.46 |
| 287-297 | VGLPSIPVHPI | 1129.38 |
| 288-297 | GLPSIPVHPI [†] | 1030.25 |
| 298-310 | GYDDAQKLLEKMG‡ | 1516.5 |
| 298-305 | GYDDAQKLS | 958.05 |
| 281-305 | RGIAEAVGLPSIPVHPIGYYDAQKL | 2666.12 |
| 281-307 | RGIAEAVGLPSIPVHPIGYYDAQKLLE | 2908.39 |
| 286-307 | AVGLPSIPVHPIGYYDAQKLLE¶ | 2381.78 |
| 287-307 | VGLPSIPVHPIGYYDAQKLLE | 2310.70 |
| 288-307 | GLPSIPVHPIGYYDAQKLLE# | 2211.57 |
| 281-299 | RGIAEAVGLPSIPVHPIGY | 1947 |
| 286-299 | AVGLPSIPVHPIGY | 1420.69 |
| 287-299 | VGLPSIPVHPIGY | 1349.61 |
| 288-299 | GLPSIPVHPIGY | 1250.48 |
| 287-310 | VGLPSIPVHPIGYYDAQKLLEKMG | 2627.14 |
| 288-310 | GLPSIPVHPIGYYDAQKLLEKMG | 2528.01 |

Boldface sequences correspond to peptides predicted to bind to MHC, see Table 10.

*By mass alone this peak could also have been 296-310 or 288-303.

**By mass alone this peak could also have been 298-307. Combination of HPLC and mass spectrometry show that at some later time points this peak is a mixture of both species.

[†] By mass alone this peak could also have been 289-298.

? By mass alone this peak could also have been 281-295 or 294-306.

§ By mass alone this peak could also have been 297-303.

¶ By mass alone this peak could also have been 285-306.

By mass alone this peak could also have been 288-303.

None of these alternate assignments are supported N-terminal pool sequence analysis.

N-terminal Pool Sequence Analysis

One aliquot at one hour of the proteasomal digestion (see Example 3 part 3 above) was subjected to N-terminal amino acid sequence analysis by an ABI 473A Protein Sequencer (Applied Biosystems, Foster City, CA). Determination of the sites and efficiencies of cleavage was based on consideration of the sequence cycle, the repetitive yield of the protein sequencer, and the relative yields of amino acids unique in the analyzed sequence. That is if the unique (in the analyzed sequence) residue X appears only in the nth cycle a cleavage site exists n-1 residues before it in the N-terminal direction. In addition to helping resolve any ambiguity in the assignment of mass to sequences, these data also provide a more reliable indication of the relative yield of the various fragments than does mass spectrometry.

For PSMA₂₈₁₋₃₁₀ (SEQ ID NO. 45) this pool sequencing supports two major cleavage sites after V₂₈₇ and I₂₉₇ among other minor cleavage sites. Reviewing the results presented in Fig. 9 reveals the following:

S at the 4th and 11th cycles indicating cleavage after V₂₈₇ and presence of the N-terminus of the substrate, respectively.

H at the 8th cycle indicating cleavage after V₂₈₇. The lack of decay in peak height at positions 9 and 10 versus the drop in height present going from 10 to 11 can suggest cleavage after A₂₈₆ and E₂₈₅ as well, rather than the peaks representing latency in the sequencing reaction.

D at the 2nd, 4th, and 7th cycles indicating cleavages after Y₂₉₉, I₂₉₇, and V₂₉₄, respectively. This last cleavage is not observed in any of the fragments in Table 10 or in the alternate assignments in the notes below.

Q at the 6th cycle indicating cleavage after I₂₉₇.

M at the 10th and 12th cycle indicating cleavages after Y₂₉₉ and I₂₉₇, respectively.

Epitope Identification

Fragments co-C-terminal with 8-10 amino acid long sequences predicted to bind HLA by the SYFPEITHI or NIH algorithms were chosen for further study. The digestion and prediction steps of the procedure can be usefully practiced in any order. Although the substrate peptide used in proteasomal digest described here was specifically designed to include a predicted HLA-A1 binding sequence, the actual products of digestion can be checked after the fact for actual or predicted binding to other MHC molecules. Selected results are shown in Table 10.

Table 10.

Predicted HLA binding by proteasomally generated fragments: PSMA₂₈₁₋₃₁₀

| SEQ ID NO. | PEPTIDE | HLA | SYFPEITHI | NIH |
|------------|--------------|-----------|-----------|------|
| 47 & (48) | (G)LPSPVHPI | A*0201 | 16 (24) | (24) |
| | | B*0702/B7 | 23 | 12 |
| | | B*5101 | 24 | 572 |
| | | Cw*0401 | NP† | 20 |
| 49 & (50) | (P)IGYYDAQKL | A*0201 | (16) | <5 |
| | | A26 | (20) | NP |
| | | B*2705 | 16 | 25 |
| | | B*2709 | 15 | NP |
| | | B*5101 | 21 | 57 |
| | | Cw*0301 | NP | 24 |
| 51 & (52) | (P)SIPVHPIGY | A1 | 21 (27) | <5 |
| | | A26 | 22 | NP |
| | | A3 | 16 | <5 |
| | | B*5101 | 16 | NP |
| 53 | IPVHPIGY | | | |
| 54 | YYDAQKLE | A1 | 22 | <5 |

†No prediction

- 5 As seen in Table 10, N-terminal addition of authentic sequence to epitopes can often generate still useful, even better epitopes, for the same or different MHC restriction elements. Note for example the pairing of (G)LPSPVHPI with HLA-A*0201, where the 10-mer can be used as a vaccine useful with several MHC types by relying on N-terminal trimming to create the epitopes for HLA-B7, -B*5101, and Cw*0401.

10 HLA-A*0201 binding assay:

HLA-A*0201 binding studies were preformed with PSMA₂₈₈₋₂₉₇, GLPSIPVHPI, (SEQ ID NO. 48) essentially as described in Examples 3 and 4 above. As seen in figure 8, this epitope exhibits significant binding at even lower concentrations than the positive control peptides.

Example 6

15 Cluster Analysis (PSMA₄₅₄₋₄₈₁).

Another peptide, SSIEGNYTLRVDCTPLMYSLVHLTKEL, PSMA₄₅₄₋₄₈₁, (SEQ ID NO. 55) containing an epitope cluster from prostate specific membrane antigen, was synthesized by MPS (purity >95%) and subjected to proteasome digestion and mass spectrum analysis as described above. Prominent peaks from the mass spectra are summarized in Table 11.

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Table 11. PSMA₄₅₄₋₄₈₁ Mass Peak Identification.

| MS PEAK (measured) | PEPTIDE | SEQUENCE | CALCULATED MASS (MH ⁺) |
|-----------------------|---------|-------------|---------------------------------------|
| 1238.5 | 454-464 | SSIEGNYTLRV | 1239.78 |

| | | | |
|--------------|-----------|---------------------------|---------|
| 1768.38±0.60 | 454-469 | SSIEGNYTLRVDCTPL | 1768.99 |
| 1899.8 | 454-470 | SSIEGNYTLRVDCTPLM | 1900.19 |
| 1097.63±0.91 | 463-471 | RVDCTPLMY | 1098.32 |
| 2062.87±0.68 | 454-471* | SSIEGNYTLRVDCTPLMY | 2063.36 |
| 1153 | 472-481** | SLVHNLTKEL | 1154.36 |
| 1449.93±1.79 | 470-481 | MYSLVHNLTKEL | 1448.73 |

Boldface sequence correspond to peptides predicted to bind to MHC, see Table 12.

* On the basis of mass alone this peak could equally well be assigned to the peptide 455-472 however proteasomal removal of just the N-terminal amino acid is considered unlikely. If the issue were important it could be resolved by N-terminal sequencing.

**On the basis of mass this fragment might also represent 455-464.

Epitope Identification

Fragments co-C-terminal with 8-10 amino acid long sequences predicted to bind HLA by the SYFPEITHI or NIH algorithms were chosen for further study. The digestion and prediction steps of the procedure can be usefully practiced in any order. Although the substrate peptide used in proteasomal digest described here was specifically designed to include predicted HLA-A2.1 binding sequences, the actual products of digestion can be checked after the fact for actual or predicted binding to other MHC molecules. Selected results are shown in Table 12.

Table 12. Predicted HLA binding by proteasomally generated fragments

| SEQ ID NO | PEPTIDE | HLA | SYFPEITHI | NIH |
|------------------|----------------|------------|------------------|------------|
| 56 & (57) | (S) IEGNYTLRV | A1 | (19) | <5 |
| 58 | EGNYTLRV | A*0201 | 16 (22) | <5 |
| | | B*5101 | 15 | NP† |
| 59 & (60) | (Y) TLRVDCTPL | A*0201 | 20 (18) | (5) |
| | | A26 | 16 (18) | NP |
| | | B7 | 14 | 40 |
| | | B8 | 23 | <5 |
| | | B*2705 | 12 | 30 |
| | | Cw*0301 | NP | (30) |
| | | | | |
| 61 | LRVDCTPLM | B*2705 | 20 | 600 |
| | | B*2709 | 20 | NP |
| 62 & (63) | (L) RVDCTPLMY | A1 | 32 (22) | 125 (13.5) |
| | | A3 | 25 | <5 |
| | | A26 | 22 | NP |
| | | B*2702 | NP | (200) |
| | | B*2705 | 13 (NP) | (1000) |

†No prediction

As seen in Table 12, N-terminal addition of authentic sequence to epitopes can often generate still useful, even better epitopes, for the same or different MHC restriction elements. Note for example the pairing of (L)RVDCTPLMY (SEQ ID NOS 62 and (63)) with HLA-B*2702/5, where the 10-mer has substantial predicted halftimes of dissociation and the co-C-

terminal 9-mer does not. Also note the case of SIEGNYTLRV (SEQ ID NO 57) a predicted HLA-A*0201 epitope which can be used as a vaccine useful with HLA-B*5101 by relying on N-terminal trimming to create the epitope.

HLA-A*0201 binding assay

5 HLA-A*0201 binding studies were preformed, essentially as described in Example 3 above, with PSMA₄₆₀₋₄₆₉, TLRVDCTPL, (SEQ ID NO. 60). As seen in figure 10, this epitope was found to bind HLA-A2.1 to a similar extent as the known A2.1 binder FLPSDYFPSV (HBV₁₈₋₂₇; SEQ ID NO: 24) used as a positive control. Additionally, PSMA₄₆₁₋₄₆₉, (SEQ ID NO. 59) binds nearly as well.

10 ELISPOT analysis: PSMA₄₆₃₋₄₇₁ (SEQ ID NO. 62)

The wells of a nitrocellulose-backed microtiter plate were coated with capture antibody by incubating overnight at 4°C using 50 µl (microliter)/well of 4µg/ml murine anti-human γ (gamma)-IFN monoclonal antibody in coating buffer (35 mM sodium bicarbonate, 15 mM sodium carbonate, pH 9.5). Unbound antibody was removed by washing 4 times 5 min. with PBS. Unbound sites on
 15 the membrane then were blocked by adding 200µl (microliter)/well of RPMI medium with 10% serum and incubating 1 hr. at room temperature. Antigen stimulated CD8⁺ T cells, in 1:3 serial dilutions, were seeded into the wells of the microtiter plate using 100µl (microliter)/well, starting at 2x10⁵ cells/well. (Prior antigen stimulation was essentially as described in Scheibenbogen, C. et al. *Int. J. Cancer* 71:932-936, 1997. PSMA₄₆₂₋₄₇₁ (SEQ ID NO. 62) was added to a final
 20 concentration of 10µg/ml and IL-2 to 100 U/ml and the cells cultured at 37°C in a 5% CO₂, water-saturated atmosphere for 40 hrs. Following this incubation the plates were washed with 6 times 200 µl (microliter)/well of PBS containing 0.05% Tween-20 (PBS-Tween). Detection antibody, 50µl (microliter)/well of 2g/ml biotinylated murine anti-human γ (gamma)-IFN monoclonal antibody in PBS+10% fetal calf serum, was added and the plate incubated at room temperature for
 25 2 hrs. Unbound detection antibody was removed by washing with 4 times 200 µl of PBS-Tween. 100µl of avidin-conjugated horseradish peroxidase (Pharmingen, San Diego, CA) was added to each well and incubated at room temperature for 1 hr. Unbound enzyme was removed by washing with 6 times 200 µl of PBS-Tween. Substrate was prepared by dissolving a 20 mg tablet of 3-amino 9-ethylcoarbasole in 2.5 ml of N, N-dimethylformamide and adding that solution to 47.5 ml of 0.05
 30 M phosphate-citrate buffer (pH 5.0). 25 µl of 30% H₂O₂ was added to the substrate solution immediately before distributing substrate at 100 µl (microliter)/well and incubating the plate at room temperature. After color development (generally 15-30 min.), the reaction was stopped by washing the plate with water. The plate was air dried and the spots counted using a stereomicroscope.

35 Figure 11 shows the detection of PSMA₄₆₃₋₄₇₁ (SEQ ID NO. 62)-reactive HLA-A1⁺ CD8⁺ T cells previously generated in cultures of HLA-A1⁺ CD8⁺ T cells with autologous dendritic cells

plus the peptide. No reactivity is detected from cultures without peptide (data not shown). In this case it can be seen that the peptide reactive T cells are present in the culture at a frequency between 1 in 2.2×10^4 and 1 in 6.7×10^4 . That this is truly an HLA-A1-restricted response is demonstrated by the ability of anti-HLA-A1 monoclonal antibody to block γ (gamma) IFN production; see figure 12.

5 Example 7

Cluster Analysis (PSMA₆₅₃₋₆₈₇).

Another peptide, FDKSNPIVLRMMNDQLMFLERAFIDPLGLPDRP FY PSMA₆₅₃₋₆₈₇, (SEQ ID NO. 64) containing an A2 epitope cluster from prostate specific membrane antigen, PSMA₆₆₀₋₆₈₁ (SEQ ID NO 65), was synthesized by MPS (purity >95%) and subjected to proteasome digestion and mass spectrum analysis as described above. Prominent peaks from the mass spectra are summarized in Table 13.

Table 13. PSMA₆₅₃₋₆₈₇ Mass Peak Identification.

| MS PEAK (measured) | PEPTIDE | SEQUENCE | CALCULATED MASS (MH ⁺) |
|-----------------------|-----------|-----------------------------|---------------------------------------|
| 906.17±0.65 | 681-687** | LPDRPFY | 908.05 |
| 1287.73±0.76 | 677-687** | DPLGLPDRPFY | 1290.47 |
| 1400.3±1.79 | 676-687 | IDPLGLPDRPFY | 1403.63 |
| 1548.0±1.37 | 675-687 | FIDPLGLPDRPFY | 1550.80 |
| 1619.5±1.51 | 674-687** | AFIDPLGLPDRPFY | 1621.88 |
| 1775.48±1.32 | 673-687* | RAFIDPLGLPDRPFY | 1778.07 |
| 2440.2±1.3 | 653-672 | FDKSNPIVLRMMNDQLMFLE | 2442.932 |
| 1904.63±1.56 | 672-687* | ERAFIDPLGLPDRPFY | 1907.19 |
| 2310.6±2.5 | 653-671 | FDKSNPIVLR MMNDQLMFL | 2313.82 |
| 2017.4±1.94 | 671-687 | LERAFIDPLGLPDRPFY | 2020.35 |
| 2197.43±1.78 | 653-670 | FDKSNPIVLR MMNDQLMF | 2200.66 |

15 **Boldface** sequence correspond to peptides predicted to bind to MHC, see Table 13.

* On the basis of mass alone this peak could equally well be assigned to a peptide beginning at 654, however proteasomal removal of just the N-terminal amino acid is considered unlikely. If the issue were important it could be resolved by N-terminal sequencing.

20 ** On the basis of mass alone these peaks could have been assigned to internal fragments, but given the overall pattern of digestion it was considered unlikely.

Epitope Identification

Fragments co-C-terminal with 8-10 amino acid long sequences predicted to bind HLA by the SYFPEITHI or NIH algorithms were chosen for further study. The digestion and prediction steps of the procedure can be usefully practiced in any order. Although the substrate peptide used in proteasomal digest described here was specifically designed to include predicted HLA-A2.1

binding sequences, the actual products of digestion can be checked after the fact for actual or predicted binding to other MHC molecules. Selected results are shown in Table 14.

Table 14. Predicted HLA binding by proteasomally generated fragments

| SEQ ID NO | PEPTIDE | HLA | SYFPEITHI | NIH |
|-----------|------------------|--------|-----------|------------|
| 66 & (67) | (R)MMNDQLMF L | A*0201 | 24 (23) | 1360 (722) |
| | | A*0205 | NP† | 71 (42) |
| | | A26 | 15 | NP |
| | | B*2705 | 12 | 50 |
| 68 | RMMNDQLMF | B*2705 | 17 | 75 |

5 †No prediction

As seen in Table 14, N-terminal addition of authentic sequence to epitopes can generate still useful, even better epitopes, for the same or different MHC restriction elements. Note for example the pairing of (R)MMNDQLMFL (SEQ ID NOS. 66 and (67)) with HLA-A*02, where the 10-mer retains substantial predicted binding potential.

HLA-A*0201 binding assay

HLA-A*0201 binding studies were preformed, essentially as described in Example 3 above, with PSMA₆₆₃₋₆₇₁, (SEQ ID NO. 66) and PSMA₆₆₂₋₆₇₁, RMMNDQLMFL (SEQ NO. 67). As seen in figures 10, 13 and 14, this epitope exhibits significant binding at even lower concentrations than the positive control peptide (FLPSDYFPSV (HBV₁₈₋₂₇); SEQ ID NO: 24). Though not run in parallel, comparison to the controls suggests that PSMA₆₆₂₋₆₇₁ (which approaches the Melan A peptide in affinity) has the superior binding activity of these two PSMA peptides.

Example 8

Vaccinating with epitope vaccines.

20 1. Vaccination with peptide vaccines:

A. Intranodal delivery

A formulation containing peptide in aqueous buffer with an antimicrobial agent, an antioxidant, and an immunomodulating cytokine, was injected continuously over several days into the inguinal lymph node using a miniature pumping system developed for insulin delivery (MiniMed; Northridge, CA). This infusion cycle was selected in order to mimic the kinetics of antigen presentation during a natural infection.

B. Controlled release

A peptide formulation is delivered using controlled PLGA microspheres as is known in the art, which alter the pharmacokinetics of the peptide and improve immunogenicity. This formulation is injected or taken orally.

C. Gene gun delivery

- 5 A peptide formulation is prepared wherein the peptide is adhered to gold microparticles as is known in the art. The particles are delivered in a gene gun, being accelerated at high speed so as to penetrate the skin, carrying the particles into dermal tissues that contain pAPCs.

D. Aerosol delivery

- 10 A peptide formulation is inhaled as an aerosol as is known in the art, for uptake into appropriate vascular or lymphatic tissue in the lungs.

2. Vaccination with nucleic acid vaccines:

- 15 A nucleic acid vaccine is injected into a lymph node using a miniature pumping system, such as the MiniMed insulin pump. A nucleic acid construct formulated in an aqueous buffered solution containing an antimicrobial agent, an antioxidant, and an immunomodulating cytokine, is delivered over a several day infusion cycle in order to mimic the kinetics of antigen presentation during a natural infection.

- Optionally, the nucleic acid construct is delivered using controlled release substances, such as PLGA microspheres or other biodegradable substances. These substances are injected or taken orally. Nucleic acid vaccines are given using oral delivery, priming the immune response through uptake into GALT tissues. Alternatively, the nucleic acid vaccines are delivered using a gene gun, wherein the nucleic acid vaccine is adhered to minute gold particles. Nucleic acid constructs can also be inhaled as an aerosol, for uptake into appropriate vascular or lymphatic tissue in the lungs.

Example 9

Assays for the effectiveness of epitope vaccines.

25 1. Tetramer analysis:

- Class I tetramer analysis is used to determine T cell frequency in an animal before and after administration of a housekeeping epitope. Clonal expansion of T cells in response to an epitope indicates that the epitope is presented to T cells by pAPCs. The specific T cell frequency is measured against the housekeeping epitope before and after administration of the epitope to an animal, to determine if the epitope is present on pAPCs. An increase in frequency of T cells specific to the epitope after administration indicates that the epitope was presented on pAPC.

2. Proliferation assay:

- 35 Approximately 24 hours after vaccination of an animal with housekeeping epitope, pAPCs are harvested from PBMCs, splenocytes, or lymph node cells, using monoclonal antibodies against specific markers present on pAPCs, fixed to magnetic beads for affinity purification. Crude blood or splenocyte preparation is enriched for pAPCs using this technique. The enriched pAPCs are

then used in a proliferation assay against a T cell clone that has been generated and is specific for the housekeeping epitope of interest. The pAPCs are coincubated with the T cell clone and the T cells are monitored for proliferation activity by measuring the incorporation of radiolabeled thymidine by T cells. Proliferation indicates that T cells specific for the housekeeping epitope are being stimulated by that epitope on the pAPCs.

3. Chromium release assay:

A human patient, or non-human animal genetically engineered to express human class I MHC, is immunized using a housekeeping epitope. T cells from the immunized subject are used in a standard chromium release assay using human tumor targets or targets engineered to express the same class I MHC. T cell killing of the targets indicates that stimulation of T cells in a patient would be effective at killing a tumor expressing a similar TuAA.

Example 10

Induction of CTL response with naked DNA is efficient by Intra-lymph node immunization.

In order to quantitatively compare the CD8⁺ CTL responses induced by different routes of immunization a plasmid DNA vaccine (pEGFP33A) containing a well-characterized immunodominant CTL epitope from the LCMV-glycoprotein (G) (gp33; amino acids 33-41) (Oehen, S., et al., *Immunology* 99, 163-169 2000) was used, as this system allows a comprehensive assessment of antiviral CTL responses. Groups of 2 C57BL/6 mice were immunized once with titrated doses (200-0.02μg) of pEGFP33A DNA or of control plasmid pEGFP-N3, administered i.m. (intramuscular), i.d. (intradermal), i.spl. (intrasplic), or i.ln. (intra-lymph node). Positive control mice received 500 pfu LCMV i.v. (intravenous). Ten days after immunization spleen cells were isolated and gp33-specific CTL activity was determined after secondary *in vitro* restimulation. As shown in Fig. 15, i.m. or i.d. immunization induced weakly detectable CTL responses when high doses of pEGFP33A DNA (200μg) were administered. In contrast, potent gp33-specific CTL responses were elicited by immunization with only 2μg pEGFP33A DNA i.spl. and with as little as 0.2μg pEGFP33A DNA given i.ln. (figure 15; symbols represent individual mice and one of three similar experiments is shown). Immunization with the control pEGFP-N3 DNA did not elicit any detectable gp33-specific CTL responses (data not shown).

Example 11

Intra-lymph node DNA immunization elicits anti-tumor immunity.

To examine whether the potent CTL responses elicited following i.ln. immunization were able to confer protection against peripheral tumors, groups of 6 C57BL/6mice were immunized three times at 6-day intervals with 10μg of pEGFP33A DNA or control pEGFP-N3 DNA. Five days after the last immunization small pieces of solid tumors expressing the gp33 epitope (EL4-33) were transplanted s.c. into both flanks and tumor growth was measured every 3-4d. Although the

EL4-33 tumors grew well in mice that had been repetitively immunized with control pEGFP-N3 DNA (figure 16), mice which were immunized with pEFGPL33A DNA i.ln. rapidly eradicated the peripheral EL4-33 tumors (figure 16).

Example 12

5 Differences in lymph node DNA content mirrors differences in CTL response following intra-lymph node and intramuscular injection.

pEFGPL33A DNA was injected i.ln. or i.m. and plasmid content of the injected or draining lymph node was assessed by real time PCR after 6, 12, 24, 48 hours, and 4 and 30 days. At 6, 12, and 24 hours the plasmid DNA content of the injected lymph nodes was approximately three orders
10 of magnitude greater than that of the draining lymph nodes following i.m. injection. No plasmid DNA was detectable in the draining lymph node at subsequent time points (Fig. 17). This is consonant with the three orders of magnitude greater dose needed using i.m. as compared to i.ln. injections to achieve a similar levels of CTL activity. CD8^{-/-} knockout mice, which do not develop a CTL response to this epitope, were also injected i.ln. showing clearance of DNA from the lymph
15 node is not due to CD8⁺ CTL killing of cells in the lymph node. This observation also supports the conclusion that i.ln. administration will not provoke immunopathological damage to the lymph node.

Example 13

Administration of a DNA plasmid formulation of a therapeutic vaccine for melanoma to humans.

20 A SYNCHROTOPE™ TA2M melanoma vaccine encoding the HLA-A2-restricted tyrosinase epitope SEQ ID NO. 1 and epitope cluster SEQ ID NO. 69, was formulated in 1% Benzyl alcohol, 1% ethyl alcohol, 0.5mM EDTA, citrate-phosphate, pH 7.6. Aliquots of 80, 160, and 320 µg DNA/ml were prepared for loading into MINIMED 407C infusion pumps. The catheter of a SILHOUETTE infusion set was placed into an inguinal lymph node visualized by
25 ultrasound imaging. The assembly of pump and infusion set was originally designed for the delivery of insulin to diabetics and the usual 17mm catheter was substituted with a 31mm catheter for this application. The infusion set was kept patent for 4 days (approximately 96 hours) with an infusion rate of about 25 µl (microliter)/hour resulting in a total infused volume of approximately 2.4 ml. Thus the total administered dose per infusion was approximately 200, and 400 µg; and can
30 be 800 µg, respectively, for the three concentrations described above. Following an infusion subjects were given a 10 day rest period before starting a subsequent infusion. Given the continued residency of plasmid DNA in the lymph node after administration (as in example 12) and the usual kinetics of CTL response following disappearance of antigen, this schedule will be sufficient to maintain the immunologic CTL response.

35 Example 14

Evaluating Likelihood of Epitope Cross-reactivity on Non-target Tissues.

As noted above PSA is a member of the kallikrein family of proteases, which is itself a subset of the serine protease family. While the members of this family sharing the greatest degree of sequence identity with PSA also share similar expression profiles, it remains possible that individual epitope sequences might be shared with proteins having distinctly different expression profiles. A first step in evaluating the likelihood of undesirable cross-reactivity is the identification of shared sequences. One way to accomplish this is to conduct a BLAST search of an epitope sequence against the SWISSPROT or Entrez non-redundant peptide sequence databases using the "Search for short nearly exact matches" option; hypertext transfer protocol accessible on the world wide web (<http://www.ncbi.nlm.nih.gov/blast/index.html>). Thus searching SEQ ID NO. 104, WVLTAAHCI, against SWISSPROT (limited to entries for homo sapiens) one finds four exact matches, including PSA. The other three are from kallikrein 1 (tissue kallikrein), and elastase 2A and 2B. While these nine amino acid segments are identical, the flanking sequences are quite distinct, particularly on the C-terminal side, suggesting that processing may proceed differently and that thus the same epitope may not be liberated from these other proteins. (Please note that kallikrein naming is confused. Thus, the kallikrein 1 [accession number P06870] is a different protein than the one [accession number AAD13817] mentioned in the paragraph on PSA above in the section on tumor-associated antigens).

This possibility can be tested in several ways. Synthetic peptides containing the epitope sequence embedded in the context of each of these proteins can be subjected to *in vitro* proteasomal digestion and analysis as described above. Alternatively, cells expressing these other proteins, whether by natural or recombinant expression, can be used as targets in a cytotoxicity (or similar) assay using CD8⁺ T cells that recognize the epitope, in order to determine if the epitope is processed and presented.

Examples 15-67

Epitopes.

The methodologies described above, and in particular in examples 3-7, have been applied to additional synthetic peptide substrates, as summarized in figures 18-70 leading to the identification of further epitopes as set forth in tables 15-67 below. The substrates used here were generally designed to identify products of housekeeping proteasomal processing that give rise to HLA-A*0201 binding epitopes, but additional MHC-binding reactivities can be predicted, as discussed above. Many such reactivities are disclosed, however, these listings are meant to be exemplary, not exhaustive or limiting. As also discussed above, individual components of the analyses can be used in varying combinations and orders. N-terminal pool sequencing which allows quantitation of various cleavages and can resolve ambiguities in the mass spectrum where necessary, can also be used to identify cleavage sites when digests of substrate yield fragments that do not fly well in MALDI-TOF mass spectrometry. Due to these advantages it was routinely used.

Although it is preferred to identify epitopes on the basis of the C-terminus of an observed fragment, epitopes can also be identified on the basis of the N-terminus of an observed fragment adjacent to the epitope.

Not all of the substrates necessarily meet the formal definition of an epitope cluster as referenced in example 3. Some clusters are so large that it was more convenient to use substrates spanning only a portion of the cluster. In other cases, substrates were extended beyond clusters meeting the formal definition to include neighboring predicted epitopes or were designed around predicted epitopes with no association with any cluster. In some instances, actual binding activity dictated what substrate was made when HLA binding activity was determined for a selection of peptides with predicted affinity, before synthetic substrates were designed.

Figures 18-70 show the results of proteasomal digestion analysis as a mapping of mass spectrum peaks onto the substrate sequence. Each figure presents an individual timepoint from the digestion judged to be representative of the overall data, however some epitopes listed in Tables 15-67 were identified based on fragments not observed at the particular timepoints illustrated. The mapping of peaks onto the sequence was informed by N-terminal pool sequencing of the digests, as noted above. Peaks possibly corresponding to more than one fragment are represented by broken lines. Nonetheless, epitope identifications are supported by unambiguous occurrence of the associated cleavage.

Example 15: Tyrosinase 171-203Table 15Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|------------|-----------------|----------|--------------------------|--------|
| | | | | SYFPEITHI | NIH |
| 171-179 | NIYDLFVWM | 108 | A0201 | 17 | 93.656 |
| | | | A26 | 25 | N/A |
| | | | A3 | 18 | <5 |
| 173-182 | YDLFVWMHYY | 109 | A1 | 17 | <5 |
| 174-182 | DLFVWMHYY | 110 | A1 | 16 | <5 |
| | | | A26 | 30 | N/A |
| | | | A3 | 16 | 27 |
| 186-194 | DALLGGSEI | 111 | A0201 | 17 | <5 |
| | | | B5101 | 26 | 440 |
| 191-200 | GSEIWRDIDF | 112 | A1 | 18 | 67.5 |
| 192-200 | SEIWRDIDF | 113 | B08 | 16 | <5 |
| 193-201 | EIWRDIDFA | 114 | A26 | 20 | N/A |

†Scores are given from the two binding prediction programs referenced above (see example 3). See also figure 18.

5

Example 16: Tyrosinase 401-427Table 16Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|------------|-----------------|----------|--------------------------|-------|
| | | | | SYFPEITHI | NIH |
| 407-416 | LQEVYPEANA | 115 | A0203 | 18 | N/A |
| 409-418 | EVYPEANAPI | 116 | A26 | 19 | N/A |
| | | | A3 | 20 | <5 |
| 410-418 | VYPEANAPI | 117 | B5101 | 15 | 6.921 |
| 411-418 | YPEANAPI | 118 | B5101 | 22 | N/A |
| 411-420 | YPEANAPIGH | 119 | A1 | 16 | <5 |
| 416-425 | APIGHNRESY | 120 | A1 | 18 | <5 |
| | | | A26 | 15 | N/A |
| 417-425 | PIGHNRESY | 121 | A1 | 16 | <5 |
| | | | A26 | 21 | N/A |
| | | | A3 | 17 | <5 |
| 417-426 | PIGHNRESYM | 122 | A26 | 19 | N/A |

†Scores are given from the two binding prediction programs referenced above (see example 3) See also figure 19.

10

Example 17: Tyrosinase 415-449Table 17Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|------------|-----------------|----------|--------------------------|-------|
| | | | | SYFPEITHI | NIH |
| 416-425 | APIGHNRESY | 120 | A1 | 18 | <5 |
| | | | A26 | 15 | N/A |
| | | | A3 | 17 | <5 |
| | | | B0702 | 15 | N/A |
| 417-425 | PIGHNRESY | 124 | A1 | 16 | <5 |
| | | | A26 | 21 | N/A |
| | | | A3 | 17 | <5 |
| 423-430 | ESYMPVFI | 125 | B5101 | 17 | N/A |
| 423-432 | ESYMPVFIPL | 126 | A26 | 18 | N/A |
| 424-432 | SYMVPFIPL | 127 | B0702 | 16 | N/A |
| 424-433 | SYMVPFIPLY | 128 | A1 | 19 | <5 |
| | | | A26 | 15 | N/A |
| 425-433 | YMVPFIPLY | 129 | A0201 | 18 | <5 |
| | | | A1 | 23 | 5 |
| | | | A26 | 17 | N/A |
| 426-434 | MVPFIPLYR | 130 | A3 | 18 | <5 |
| 426-435 | MVPFIPLYRN | 131 | A26 | 16 | N/A |
| 427-434 | VPIPLYR | 132 | B5101 | 18 | N/A |
| 430-437 | IPLYRNGD | 133 | B08 | 16 | <5 |
| 430-439 | IPLYRNGDFF | 134 | B0702 | 18 | N/A |
| 431-439 | PLYRNGDFF | 135 | A26 | 18 | N/A |
| | | | A3 | 24 | <5 |
| 431-440 | PLYRNGDFFI | 136 | A0201 | 16 | 23.43 |
| | | | A3 | 17 | <5 |
| 434-443 | RNGDFFISSK | 137 | A3 | 20 | <5 |
| 435-443 | NGDFFISSK | 138 | A3 | 15 | <5 |
| | | | B2705 | 15 | 5 |

5 †Scores are given from the two binding prediction programs referenced above (see example 3). See also figure 20.

Example 18: Tyrosinase 457-484Table 18Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|------------|-----------------|----------|--------------------------|-------|
| | | | | SYFPEITHI | NIH |
| 463-471 | YIKSYLEQA | 139 | A0201 | 18 | <5 |
| | | | A26 | 17 | N/A |
| 466-474 | SYLEQASRI | 140 | B5101 | 16 | <5 |
| 469-478 | EQASRIWSWL | 141 | A26 | 17 | N/A |
| 470-478 | QASRIWSWL | 142 | B5101 | 16 | 55 |
| 471-478 | ASRIWSWL | 143 | B08 | 16 | <5 |
| 471-479 | ASRIWSWLL | 144 | B08 | 16 | <5 |
| 473-481 | RIWSWLLGA | 145 | A0201 | 19 | 13.04 |
| | | | A26 | 16 | N/A |
| | | | A3 | 15 | <5 |

10 †Scores are given from the two binding prediction programs referenced above (see example 3). See also figure 21.

Example 19: CEA 92-118

Table 19

Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|------------|-----------------|----------|--------------------------|--------|
| | | | | SYFPEITHI | NIH |
| 92-100 | GPAYSGREI | 146 | B0702 | 18 | 8 |
| | | | B08 | 15 | <5 |
| | | | B5101 | 22 | 484 |
| 92-101 | GPAYSGREII | 147 | B0702 | 18 | 12 |
| 93-100 | PAYSGREI | 148 | B5101 | 22 | N.A. |
| 93-101 | PAYSGREII | 149 | B5101 | 24 | 48.4 |
| 93-102 | PAYSGREIY | 150 | A1 | 19 | <5 |
| 94-102 | AYSGREIY | 151 | A1 | 21 | <5 |
| 97-105 | GREIYPNA | 152 | B2705 | 17 | 200 |
| | | | B2709 | 16 | |
| 98-107 | REIYPNASL | 153 | A0201 | 16 | <5 |
| 99-107 | EIYPNASL | 154 | A0201 | 21 | <5 |
| | | | A26 | 28 | N.A. |
| | | | A3 | 16 | <5 |
| | | | B0702 | 15 | 6 |
| | | | B08 | 18 | <5 |
| | | | B2705 | 16 | <5 |
| 99-108 | EIYPNASLL | 155 | A0201 | 16 | <5 |
| | | | A26 | 27 | N.A. |
| | | | A3 | 17 | <5 |
| 100-107 | IYPNASL | 156 | B08 | 15 | <5 |
| 100-108 | IYPNASLL | 157 | A0201 | 23 | 15.979 |
| | | | A26 | 21 | N.A. |
| | | | A24 | N.A. | <5 |
| | | | A3 | 23 | <5 |
| | | | B08 | 15 | <5 |
| | | | B1510 | 15 | N.A. |
| | | | B2705 | 16 | 50 |
| | | | B2709 | 15 | |
| 100-109 | IYPNASLLI | 158 | A0201 | 22 | 7.804 |
| | | | A3 | 20 | <5 |
| 102-109 | YPNASLLI | 159 | B5101 | 23 | N.A. |
| 107-116 | LLIQNIQND | 160 | A0201 | 18 | <5 |
| | | | A26 | 17 | N.A. |

5

†Scores are given from the two binding prediction programs referenced above (see example 3). See also figure 22.

Example 20: CEA 131-159Table 20Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|------------|-----------------|----------|--------------------------|------|
| | | | | SYFPEITHI | NIH |
| 132-141 | EEATGQFRVY | 161 | A1 | 19 | <5 |
| | | | A26 | 21 | N.A. |
| 133-141 | EATGQFRVY | 162 | A1 | 22 | <5 |
| | | | A26 | 23 | N.A. |
| | | | B5101 | 16 | <5 |
| 141-149 | YPELPKPSI | 163 | B0702 | 20 | <5 |
| | | | B5101 | 22 | 572 |
| 142-149 | PELPKPSI | 164 | B08 | 16 | <5 |

†Scores are given from the two binding prediction programs referenced above (see example 3). See also figure 23.

5

Example 21: CEA 225-251Table 21Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|------------|-----------------|----------|--------------------------|--------|
| | | | | SYFPEITHI | NIH |
| 225-233 | RSDSVILNV | 165 | A0201 | 15 | <5 |
| | | | A1 | 22 | <5 |
| | | | B2709 | 15 | N.A. |
| 225-234 | RSDSVILNVL | 166 | A0201 | 15 | <5 |
| 226-234 | SDSVILNVL | 167 | A0201 | 17 | <5 |
| 226-235 | SDSVILNVLY | 168 | A1 | 20 | <5 |
| 227-235 | DSVILNVLY | 169 | A1 | 22 | <5 |
| | | | A26 | 18 | N.A. |
| 233-242 | VLYGPDAPTI | 170 | A0201 | 25 | 56.754 |
| | | | A3 | 23 | <5 |
| 234-242 | LYGPDAPTI | 171 | A0201 | 15 | <5 |
| | | | B5101 | 15 | 5.72 |
| 235-242 | YGPDAPTI | 172 | B5101 | 22 | N.A. |
| 236-245 | GPDAPTISPL | 173 | A0201 | 15 | <5 |
| | | | B0702 | 23 | 24 |
| 237-245 | PDAPTISPL | 174 | A0201 | 15 | <5 |
| | | | A26 | 16 | N.A. |
| | | | B2705 | 15 | <5 |
| 238-245 | DAPTISPL | 175 | B5101 | 25 | N.A. |
| 239-247 | APTISPLNT | 176 | B0702 | 20 | 6 |
| 240-249 | PTISPLNTSY | 177 | A1 | 22 | <5 |
| | | | A26 | 24 | N.A. |
| 241-249 | TISPLNTSY | 178 | A1 | 20 | 5 |
| | | | A26 | 24 | N.A. |
| | | | A3 | 20 | <5 |

†Scores are given from the two binding prediction programs referenced above (see example 3). See also figure 24.

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Example 22: CEA 239-270Table 22Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|------------|-----------------|----------|--------------------------|------|
| | | | | SYFPEITHI | NIH |
| 240-249 | PTISPLNTSY | 179 | A1 | 22 | <5 |
| | | | A26 | 24 | N.A. |
| 241-249 | TISPLNTSY | 180 | A1 | 20 | 5 |
| | | | A26 | 24 | N.A. |
| | | | A3 | 20 | <5 |
| 246-255 | NTSYRSGENL | 181 | A26 | 19 | N.A. |
| 247-255 | TSYRSGENL | 182 | B2705 | 15 | 50 |
| 248-255 | SYRSGENL | 183 | B08 | 18 | <5 |
| 248-257 | SYRSGENLNL | 184 | B0702 | 14 | <5 |
| 249-257 | YRSGENLNL | 185 | A0201 | 15 | <5 |
| | | | B0702 | 16 | <5 |
| | | | B2705 | 27 | 2000 |
| | | | B2709 | 22 | N.A. |
| 251-259 | SGENLNLSC | 186 | A1 | 19 | <5 |
| 253-262 | ENLNLSCHAA | 187 | A0203 | 19 | <5 |
| 254-262 | NLNLSCHAA | 188 | A0201 | 17 | <5 |

5 †Scores are given from the two binding prediction programs referenced above (see example 3). See also figure 25.

Example 23: CEA 259-28610 Table 23Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|------------|-----------------|----------|--------------------------|------|
| | | | | SYFPEITHI | NIH |
| 260-269 | HAASNPPAQY | 189 | A1 | 15 | <5 |
| 261-269 | AASNPPAQY | 190 | A1 | 17 | <5 |
| | | | A3 | 17 | <5 |
| 264-273 | NPPAQYSWFV | 191 | B0702 | 18 | <5 |
| 265-273 | PPAQYSWFV | 192 | B0702 | 18 | <5 |
| | | | B5101 | 19 | 20 |
| 266-273 | PAQYSWFV | 193 | B5101 | 18 | N.A. |
| 272-280 | FVNGTFQQS | 194 | A26 | 18 | N.A. |
| | | | A3 | 15 | <5 |

†Scores are given from the two binding prediction programs referenced above (see example 3). See also figure 26.

Example 24: CEA 309-336Table 24Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|------------|-----------------|----------|--------------------------|------|
| | | | | SYFPEITHI | NIH |
| 310-319 | RTTVTTITVY | 195 | A1 | 22 | <5 |
| | | | A26 | 24 | N.A. |
| | | | A3 | 15 | <5 |
| 311-319 | TTVTTITVY | 196 | A1 | 22 | <5 |
| | | | A26 | 24 | N.A. |
| | | | B2705 | 15 | 5 |
| 319-327 | YAEPPKPFI | 197 | A0201 | 17 | <5 |
| | | | A1 | 17 | 18 |
| | | | B5101 | 22 | 286 |
| 319-328 | YAEPPKPFIT | 198 | A1 | 16 | 45 |
| 320-327 | AEPPKPFI | 199 | B08 | 16 | <5 |
| 321-328 | EPPKPFIT | 200 | B5101 | 16 | N.A. |
| 321-329 | EPPKPFITS | 201 | B0702 | 16 | <5 |
| | | | B5101 | 16 | 12.1 |
| 322-329 | PPKPFITS | 202 | B08 | 16 | <5 |

5 †Scores are given from the two binding prediction programs referenced above (see example 3). See also figure 27.

Example 25: CEA 381-408Table 2510 Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|------------|-----------------|----------|--------------------------|------|
| | | | | SYFPEITHI | NIH |
| 382-391 | SVTRNDVGPY | 203 | A1 | 18 | <5 |
| | | | A26 | 24 | N.A. |
| | | | A3 | 21 | <5 |
| 383-391 | VTRNDVGPY | 204 | A1 | 23 | <5 |
| | | | A26 | 24 | N.A. |
| 389-397 | GPYECGIQN | 205 | B5101 | 17 | 11 |
| 391-399 | YECGIQNEL | 206 | A0201 | 17 | <5 |
| | | | B2705 | 17 | 30 |
| 394-402 | GIQNELSVD | 207 | A26 | 15 | N.A. |
| | | | A3 | 16 | <5 |

†Scores are given from the two binding prediction programs referenced above (see example 3). See also figure 28.

Example 26: CEA 403-429Table 265 Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|------------|-----------------|----------|--------------------------|--------|
| | | | | SYFPEITHI | NIH |
| 403-411 | HSDPVILNV | 208 | A0201 | 17 | <5 |
| | | | A1 | 26 | 37.5 |
| 403-412 | HSDPVILNVL | 209 | A0201 | 17 | <5 |
| | | | A1 | 19 | 7.5 |
| | | | A26 | 15 | N.A. |
| | | | A24 | N.A. | 8.064 |
| | | | B4402 | 17 | N.A. |
| 404-412 | SDPVILNVL | 210 | A0201 | 17 | <5 |
| | | | B4402 | 16 | N.A. |
| 404-413 | SDPVILNVLY | 211 | A1 | 20 | <5 |
| 405-412 | DPVILNVL | 212 | B08 | 16 | <5 |
| | | | B5101 | 24 | N.A. |
| 405-413 | DPVILNVLY | 213 | A1 | 18 | <5 |
| | | | A26 | 18 | N.A. |
| | | | B5101 | 16 | 7.26 |
| 408-417 | ILNVLYGPDD | 214 | A3 | 15 | <5 |
| 411-420 | VLYGPDDPTI | 215 | A0201 | 25 | 56.754 |
| | | | A3 | 20 | <5 |
| 412-420 | LYGPDDPTI | 216 | A0201 | 15 | <5 |
| | | | A24 | N.A. | 60 |
| 413-420 | YGPDDPTI | 217 | B5101 | 22 | N.A. |
| 417-425 | DPTISPSYT | 218 | B0702 | 16 | <5 |
| 418-427 | PTISPSYTTY | 219 | A1 | 21 | <5 |
| | | | A26 | 27 | N.A. |
| 419-427 | TISPSYTTY | 220 | A1 | 19 | 5 |
| | | | A26 | 27 | N.A. |

†Scores are given from the two binding prediction programs referenced above (see example 3). See also figure 29.

Example 27: CEA 416-448

Table 27

Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|------------|-----------------|----------|--------------------------|------|
| | | | | SYFPEITHI | NIH |
| 418-427 | PTISPSYTTY | 221 | A1 | 21 | <5 |
| | | | A26 | 27 | N.A. |
| 419-427 | TISPSYTTY | 222 | A1 | 19 | 5 |
| | | | A26 | 27 | N.A. |
| | | | A3 | 18 | <5 |
| 419-428 | TISPSYTYR | 223 | A3 | 15 | 5.4 |
| 424-433 | YTYRPGVNL | 224 | A0201 | 18 | <5 |
| | | | A24 | N.A. | <5 |
| | | | A26 | 20 | N.A. |
| 425-433 | TYRPGVNL | 225 | A0201 | 14 | <5 |
| | | | A24 | N.A. | 200 |
| | | | B0702 | 16 | <5 |
| | | | B2705 | 16 | 5 |
| 426-433 | YYRPGVNL | 226 | B08 | 16 | <5 |
| 426-435 | YYRPGVNLSL | 227 | A0201 | 17 | <5 |
| | | | B0702 | 15 | <5 |
| 427-435 | YRPGVNLSL | 228 | A0201 | 17 | <5 |
| | | | B2705 | 26 | 2000 |
| | | | B2709 | 21 | N.A. |
| 428-435 | RPGVNLSL | 229 | B08 | 17 | <5 |
| | | | B5101 | 17 | N.A. |
| 428-437 | RPGVNLSLSC | 230 | B0702 | 14 | <5 |
| 430-438 | GVNLSLSCH | 231 | A26 | 16 | N.A. |
| | | | B2705 | 15 | <5 |
| 431-440 | VNLSLSCHAA | 232 | A0203 | 19 | N.A. |
| 432-440 | NLSLSCHAA | 233 | A0201 | 16 | <5 |

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† Scores are given from the two binding prediction programs referenced above (see example 3). See also figure 30.

Example 28: CEA 437-464Table 28Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|------------|-----------------|----------|--------------------------|------|
| | | | | SYFPEITHI | NIH |
| 438-447 | HAASNPPAQY | 234 | A1 | 15 | <5 |
| 439-447 | AASNPPAQY | 235 | A1 | 17 | <5 |
| | | | A3 | 17 | <5 |
| 442-451 | NPPAQYSWLI | 236 | B0702 | 17 | 8 |
| 443-451 | PPAQYSWLI | 237 | B0702 | 17 | <5 |
| | | | B5101 | 21 | 40 |
| 444-451 | PAQYSWLI | 238 | B5101 | 20 | N.A. |
| 449-458 | WLIDGNIQQH | 239 | A0201 | 17 | <5 |
| | | | A26 | 17 | N.A. |
| | | | A3 | 21 | <5 |
| 450-458 | LIDGNIQQH | 240 | A0201 | 16 | <5 |
| | | | A26 | 19 | N.A. |
| | | | A3 | 17 | <5 |
| 450-459 | LIDGNIQQHT | 241 | A0201 | 16 | <5 |
| | | | A26 | 15 | N.A. |

5 †Scores are given from the two binding prediction programs referenced above (see example 3). See also figure 31.

Example 29: CEA 581-607Table 29Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|------------|-----------------|----------|--------------------------|--------|
| | | | | SYFPEITHI | NIH |
| 581-590 | RSDPVTLDVL | 242 | A0201 | 16 | <5 |
| | | | A1 | 19 | 7.5 |
| | | | A26 | 15 | N.A. |
| | | | A24 | N.A. | 9.6 |
| 582-590 | SDPVTLDVL | 243 | A0201 | 16 | <5 |
| 582-591 | SDPVTLDVLY | 244 | A1 | 19 | <5 |
| 583-590 | DPVTLDVL | 245 | B08 | 16 | <5 |
| | | | B5101 | 25 | N.A. |
| 583-591 | DPVTLDVLY | 246 | A1 | 17 | <5 |
| | | | A26 | 18 | N.A. |
| | | | B5101 | 16 | 6 |
| 588-597 | DVLYGPDTPi | 247 | A26 | 16 | N.A. |
| 589-597 | VLYGPDTPi | 248 | A0201 | 25 | 56.754 |
| | | | A3 | 17 | 6.75 |
| | | | B5101 | 17 | 11.44 |
| 596-605 | PIISPPDSSY | 249 | A1 | 15 | <5 |
| | | | A26 | 25 | N.A. |
| | | | A3 | 22 | <5 |
| 597-605 | IISPPDSSY | 250 | A1 | 20 | 5 |
| | | | A26 | 24 | N.A. |
| | | | A3 | 24 | <5 |

10 †Scores are given from the two binding prediction programs referenced above (see example 3). See also figure 32.

Example 30: CEA 595-622Table 30Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|------------|-----------------|----------|--------------------------|--------|
| | | | | SYFPEITHI | NIH |
| 597-606 | IISPPDSSYL | 251 | A0201 | 22 | 27.464 |
| | | | A26 | 21 | N.A. |
| | | | A3 | 16 | <5 |
| | | | B0702 | 14 | <5 |
| 599-606 | SPPDSSYL | 252 | B08 | 18 | <5 |
| | | | B5101 | 17 | N.A. |
| 600-608 | PPDSSYLSG | 253 | A1 | 16 | <5 |
| 600-609 | PPDSSYLSGA | 254 | B0702 | 17 | <5 |
| 602-611 | DSSYLSGANL | 255 | A26 | 16 | N.A. |
| 603-611 | SSYLSGANL | 256 | A0201 | 15 | <5 |
| | | | B2705 | 17 | 50 |
| 604-613 | SYLSGANLNL | 257 | A0201 | 15 | <5 |
| | | | A24 | N.A. | 300 |
| 605-613 | YLSGANLNL | 258 | A0201 | 25 | 98.267 |
| | | | A26 | 19 | N.A. |
| | | | A3 | 15 | <5 |
| | | | B0702 | 16 | <5 |
| | | | B08 | 17 | <5 |
| | | | B2705 | 16 | 30 |
| 610-618 | NLNLCHSA | 259 | A0201 | 18 | <5 |

5 †Scores are given from the two binding prediction programs referenced above (see example 3) See also figure 33.

Example 31: CEA 615-641Table 3110 Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|------------|-----------------|----------|--------------------------|-------|
| | | | | SYFPEITHI | NIH |
| 620-629 | NPSPQYSWRI | 260 | B0702 | 19 | 8 |
| 622-629 | SPQYSWRI | 261 | B08 | 15 | <5 |
| | | | B5101 | 20 | N.A. |
| 627-635 | WRINGIPQQ | 262 | B2705 | 19 | 20 |
| 628-636 | RINGIPQQH | 263 | A3 | 22 | <5 |
| | | | B2705 | 16 | <5 |
| 628-637 | RINGIPQQHT | 264 | A0201 | 15 | <5 |
| 631-639 | GIPQQHTQV | 265 | A0201 | 19 | 9.563 |
| 632-639 | IPQQHTQV | 266 | B5101 | 20 | N.A. |

†Scores are given from the two binding prediction programs referenced above (see example 3). See also figure 34.

Example 32: CEA 643-677Table 32Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|------------|-----------------|----------|--------------------------|------|
| | | | | SYFPEITHI | NIH |
| 644-653 | KITPNNNGTY | 267 | A1 | 20 | 5 |
| | | | A26 | 22 | N.A. |
| | | | A3 | 25 | <5 |
| 645-653 | ITPNNNGTY | 268 | A1 | 22 | <5 |
| | | | A26 | 21 | N.A. |
| | | | A3 | 14 | <5 |
| 647-656 | PNNNGTYACF | 269 | A26 | 15 | N.A. |
| 648-656 | NNNGTYACF | 270 | A26 | 17 | N.A. |
| 650-657 | NGTYACFV | 271 | B5101 | 15 | N.A. |
| 661-670 | ATGRNNSIVK | 272 | A3 | 20 | <5 |
| 662-670 | TGRNNSIVK | 273 | A3 | 18 | <5 |
| 664-672 | RNNSIVKSI | 274 | B2709 | 15 | N.A. |
| 666-674 | NSIVKSITV | 275 | A0201 | 16 | <5 |

5 †Scores are given from the two binding prediction programs referenced above (see example 3). See also figure 35.

Example 33: GAGE-1 6-3210 Table 33Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|------------|-----------------|----------|--------------------------|-----|
| | | | | SYFPEITHI | NIH |
| 7-16 | STYRPRPRRY | 276 | A1 | 23 | <5 |
| | | | A26 | 21 | N/A |
| | | | A3 | 15 | <5 |
| 8-16 | TYRPRPRRY | 277 | A1 | 19 | <5 |
| | | | A3 | 15 | <5 |
| | | | A3 | 17 | <5 |
| 10-18 | RPRPRRYVE | 278 | B0702 | 16 | N/A |
| | | | B08 | 20 | <5 |
| | | | B5101 | 15 | N/A |
| 16-23 | YVEPPEMI | 279 | B5101 | 15 | N/A |
| 22-31 | MIGPMRPEQF | 280 | A26 | 23 | N/A |
| | | | A3 | 19 | <5 |
| 23-31 | IGPMRPEQF | 281 | B08 | 15 | <5 |
| 24-31 | GPMRPEQF | 282 | B5101 | 16 | N/A |

†Scores are given from the two binding prediction programs referenced above (see example 3). See also figure 36.

Example 34: GAGE-1 105-131Table 345 Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|------------|-----------------|----------|--------------------------|---------|
| | | | | SYFPEITHI | NIH |
| 105-114 | KTPEEEMRSH | 283 | A26 | 18 | N/A |
| 106-115 | TPEEEMRSHY | 284 | A1 | 26 | 11.25 |
| 107-115 | PEEEMRSHY | 285 | A1 | 26 | <5 |
| 110-119 | EMRSHYVAQT | 286 | A0201 | 15 | <5 |
| 113-121 | SHYVAQTGI | 287 | B5101 | 15 | <5 |
| 115-124 | YVAQTGILWL | 288 | A0201 | 23 | 108.769 |
| | | | A26 | 24 | N/A |
| | | | A3 | 15 | <5 |
| 116-124 | VAQTGILWL | 289 | A0201 | 22 | 6.381 |
| | | | B08 | 16 | <5 |
| | | | B2705 | 16 | 10 |
| | | | B5101 | 20 | 78.65 |
| 116-125 | VAQTGILWLL | 290 | A0201 | 19 | 8.701 |
| 117-125 | AQTGILWLL | 291 | A0201 | 17 | 37.362 |
| | | | B2705 | 16 | 200 |
| 118-126 | QTGILWLLM | 292 | A26 | 19 | N/A |
| 118-127 | QTGILWLLMN | 293 | A26 | 15 | N/A |
| 120-129 | GILWLLMNNC | 294 | A26 | 15 | N/A |
| 121-129 | ILWLLMNNC | 295 | A0201 | 15 | 161.227 |

†Scores are given from the two binding prediction programs referenced above (see example 3). See also figure 37.

Example 35: GAGE-1 112-137Table 35Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|------------|-----------------|----------|--------------------------|----------|
| | | | | SYFPEITHI | NIH |
| 124-131 | LLMNNCFL | 296 | B08 | 16 | <5 |
| 123-131 | WLLMNNCFL | 297 | A0201 | 22 | 1999.734 |
| | | | A26 | 16 | N/A |
| | | | B08 | 17 | <5 |
| 122-130 | LWLLMNNCF | 298 | B2705 | 15 | <5 |
| 121-130 | ILWLLMNNCF | 299 | A26 | 18 | N/A |
| | | | A3 | 17 | 10 |
| 121-129 | ILWLLMNNC | 295 | A0201 | 15 | 161.227 |
| 120-129 | GILWLLMNNC | 294 | A26 | 15 | N/A |
| 118-127 | QTGILWLLMN | 293 | A26 | 15 | N/A |
| 118-126 | QTGILWLLM | 292 | A26 | 19 | N/A |
| 117-125 | AQTGILWLL | 291 | A0201 | 17 | 37.362 |
| | | | B2705 | 16 | 200 |
| | | | B4402 | 17 | N/A |
| 116-125 | VAQTGILWLL | 290 | A0201 | 19 | 8.701 |
| 116-124 | VAQTGILWL | 289 | A0201 | 22 | 6.381 |
| | | | B08 | 16 | <5 |
| | | | B2705 | 16 | 10 |
| | | | B4402 | 15 | N/A |
| | | | B5101 | 20 | 78.65 |
| 115-124 | YVAQTGILWL | 288 | A0201 | 23 | 108.769 |
| | | | A26 | 24 | N/A |
| | | | A3 | 15 | <5 |
| 113-121 | SHYVAQTGI | 287 | B5101 | 15 | <5 |

†Scores are given from the two binding prediction programs referenced above (see example 3). See also figure 38.

Example 36 MAGE-1 51-77Table 36Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|------------|-----------------|----------|--------------------------|-----|
| | | | | SYFPEITHI | NIH |
| 62-70 | SAFPTTINF | 309 | A26 | 15 | N/A |
| | | | B4402 | 18 | N/A |
| | | | B2705 | 17 | 25 |
| 61-70 | ASAFPTTINF | 310 | B4402 | 15 | N/A |
| 60-68 | GASAFPTTI | 311 | A0201 | 16 | <5 |
| | | | B5101 | 25 | 220 |
| 57-66 | SPQGASAFPT | 312 | B0702 | 19 | N/A |

†Scores are given from the two binding prediction programs referenced above. See also figure 39.

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Example 37: Mage-1 126-153Table 37Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|------------|-----------------|----------|--------------------------|-----|
| | | | | SYFPEITHI | NIH |
| 144-151 | FGKASESL | 313 | B08 | 21 | <5 |
| 143-151 | IFGKASESL | 314 | A26 | 16 | N/A |
| | | | B2705 | 15 | <5 |
| 142-151 | EIFGKASESL | 315 | A0201 | 20 | <5 |
| | | | A26 | 29 | N/A |
| | | | B4402 | 15 | N/A |
| 142-149 | EIFGKASE | 316 | B08 | 16 | <5 |
| 133-140 | IKNYKHCF | 317 | B08 | 18 | <5 |
| 132-140 | VIKNYKHCF | 318 | A26 | 21 | N/A |
| | | | B08 | 21 | <5 |
| 131-140 | SVIKNYKHCF | 319 | A26 | 23 | N/A |
| | | | A3 | 18 | <5 |
| | | | B4402 | 15 | N/A |
| 132-139 | VIKNYKHC | 320 | B08 | 15 | <5 |
| 131-139 | SVIKNYKHC | 321 | A26 | 18 | N/A |
| 128-136 | MLESVIKNY | 322 | A1 | 28 | 45 |
| | | | A26 | 24 | N/A |
| | | | A3 | 17 | <5 |
| | | | B4402 | 15 | N/A |
| 127-136 | EMLESVIKNY | 323 | A1 | 15 | <5 |
| | | | A26 | 23 | N/A |
| | | | B4402 | 18 | N/A |
| 126-134 | AEMLESVIK | 324 | A3 | 18 | <5 |
| | | | B2705 | 15 | 30 |
| | | | B4402 | 16 | N/A |

†Scores are given from the two binding prediction programs referenced above (see example 3). See also figure 40.

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Example 38: MAGE-2 272-299Table 385 Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions [†] | |
|---------|----------------|-----------------|----------|--------------------------------------|---------|
| | | | | SYFPEITHI | NIH |
| 274-283 | GPRALIETSY | 325 | A1 | 15 | <5 |
| 275-283 | PRALIETSY | 326 | A1 | 15 | <5 |
| | | | B2705 | 23 | 100 |
| 276-284 | RALIETSYV | 327 | A0201 | 18 | 19.658 |
| | | | B5101 | 20 | 55 |
| 277-286 | ALIETSYVKV | 328 | A0201 | 30 | 427.745 |
| | | | A26 | 18 | N/A |
| | | | A3 | 21 | <5 |
| 278-286 | LIETSYVKV | 329 | A0201 | 23 | <5 |
| | | | A26 | 17 | N/A |
| | | | B5101 | 15 | <5 |
| 278-287 | LIETSYVKVL | 330 | A0201 | 22 | <5 |
| | | | A26 | 22 | N/A |
| 279-287 | IETSYVKVL | 331 | A0201 | 15 | <5 |
| | | | B1510 | 15 | N/A |
| | | | B5101 | 15 | <5 |
| 280-289 | ETSYVKVLH H | 332 | A26 | 21 | N/A |
| 282-291 | SYVKVLHHT L | 333 | A0201 | 15 | <5 |
| 283-291 | YVKVLHHTL | 334 | A0201 | 19 | <5 |
| | | | A26 | 20 | N/A |
| | | | A3 | 15 | <5 |
| | | | B08 | 21 | <5 |
| 285-293 | KVLHHTLKI | 335 | A0201 | 20 | 11.822 |
| | | | A3 | 18 | <5 |
| | | | B5101 | 15 | <5 |

[†]Scores are given from the two binding prediction programs referenced above (see example 3).] See also figure 41.

Example 39 MAGE-2 287-314Table 39Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|------------|-----------------|----------|--------------------------|-----|
| | | | | SYFPEITHI | NIH |
| 303-311 | PLHERALRE | 336 | A3 | 19 | <5 |
| | | | B08 | 16 | <5 |
| 302-309 | PPLHERAL | 337 | B08 | 16 | <5 |
| | | | B5101 | 18 | N/A |
| 301-309 | YPPLHERAL | 338 | B0702 | 21 | N/A |
| | | | B08 | 18 | <5 |
| | | | B4402 | 15 | N/A |
| | | | B5101 | 20 | 143 |
| 300-309 | SYPPLHERAL | 339 | A0201 | 15 | <5 |
| | | | B4402 | 18 | N/A |
| 299-307 | ISYPPLHER | 340 | B2705 | 17 | 25 |
| 298-307 | HISYPPLHER | 341 | A26 | 15 | N/A |
| 292-299 | KIGGEPHI | 342 | B5101 | 15 | N/A |
| 291-299 | LKIGGEPHI | 343 | A0201 | 17 | <5 |
| 290-299 | TLKIGGEPHI | 344 | A0201 | 18 | <5 |

†Scores are given from the two binding prediction programs referenced above (see example 3). See also figure 42.

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Example 40 Mage-3 287-314Table 40Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|------------|-----------------|----------|--------------------------|-------|
| | | | | SYFPEITHI | NIH |
| 303-311 | PLHEWVLRE | 345 | A26 | 15 | N/A |
| 302-309 | PPLHEWVL | 346 | B08 | 16 | <5 |
| | | | B5101 | 19 | N/A |
| 301-309 | YPPLHEWVL | 347 | B0702 | 21 | N/A |
| | | | B08 | 17 | <5 |
| | | | B5101 | 22 | 130 |
| 301-308 | YPPLHEWV | 348 | B5101 | 22 | N/A |
| 300-308 | SYPPLHEWV | 349 | A0201 | 15 | <5 |
| 299-308 | ISYPPLHEWV | 350 | A0201 | 15 | 6.656 |
| 298-307 | HISYPPLHEW | 351 | A26 | 15 | N/A |
| 293-301 | ISGGPHISY | 352 | A1 | 25 | <5 |
| 292-301 | KISGGPHISY | 353 | A1 | 20 | <5 |
| | | | A26 | 23 | N/A |
| | | | A3 | 21 | 5.4 |

†Scores are given from the two binding prediction programs referenced above (see example 3). See also figure 43.

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Example 41: Melan-A 44-71Table 415 Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|----------------|-----------------|----------|--------------------------|----------|
| | | | | SYFPEITH I | NIH |
| 45-54 | CWYCRRRNG Y | 354 | A1 | 16 | <5 |
| 46-54 | WYCRRRNGY | 355 | A1 | 16 | <5 |
| 47-55 | YCRRRNGYR | 356 | B08 | 15 | <5 |
| 49-57 | RRRNGYRAL | 357 | B08 | 17 | <5 |
| | | | B2705 | 26 | 1800 |
| | | | B2709 | 24 | N/A |
| 51-60 | RNGYRALMD K | 358 | A3 | 15 | <5 |
| 52-60 | NGYRALMDK | 359 | A3 | 18 | <5 |
| 55-63 | RALMDKSLH | 360 | B2705 | 16 | <5 |
| 56-63 | ALMDKSLH | 361 | B08 | 16 | <5 |
| 55-64 | RALMDKSLH V | 362 | A0201 | 17 | <5 |
| 56-64 | ALMDKSLHV | 363 | A0201 | 26 | 1055.104 |
| | | | A3 | 18 | <5 |
| | | | B08 | 16 | <5 |

†Scores are given from the two binding prediction programs referenced above (see example 3). See also figure 44.

Example 42: PRAME 274-301Table 42Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|------------|-----------------|----------|--------------------------|--------|
| | | | | SYFPEITH I | NIH |
| 275-284 | YISPEKEEQY | 364 | A1 | 21 | 5 |
| | | | A26 | 23 | N/A |
| | | | A3 | 20 | <5 |
| | | | B4402 | 15 | N/A |
| 276-284 | ISPEKEEQY | 365 | A1 | 19 | <5 |
| | | | A26 | 15 | N/A |
| 277-285 | SPEKEEQYI | 366 | B0702 | 17 | N/A |
| | | | B5101 | 21 | 484 |
| 278-285 | PEKEEQYI | 367 | B08 | 18 | <5 |
| 279-288 | EKEEQYIAQF | 368 | A26 | 24 | N/A |
| | | | B4402 | 16 | N/A |
| 280-288 | KEEQYIAQF | 369 | A26 | 17 | N/A |
| | | | B2705 | 19 | 45 |
| | | | B4402 | 25 | N/A |
| 283-292 | QYIAQFTSQF | 370 | A3 | 17 | <5 |
| | | | B4402 | 15 | N/A |
| 284-292 | YIAQFTSQF | 371 | A0201 | 15 | <5 |
| | | | A26 | 24 | N/A |
| | | | A3 | 19 | <5 |
| 284-293 | YIAQFTSQFL | 372 | A0201 | 22 | 74.314 |
| | | | A26 | 21 | N/A |
| 285-293 | IAQFTSQFL | 373 | A0201 | 15 | <5 |
| | | | B08 | 15 | <5 |
| | | | B5101 | 19 | 78.65 |
| 286-295 | AQFTSQFLSL | 374 | A0201 | 16 | 15.226 |
| | | | A26 | 15 | N/A |
| | | | B0702 | 15 | N/A |
| | | | A4402 | 18 | N/A |
| 287-295 | QFTSQFLSL | 375 | A26 | 21 | N/A |
| 290-298 | SQFLSLQCL | 376 | A0201 | 17 | 18.432 |
| | | | A26 | 16 | N/A |
| | | | B2705 | 16 | 1000 |
| | | | B4402 | 15 | N/A |

†Scores are given from the two binding prediction programs referenced above (see example 3). See also figure 45.

Example 43: PRAME 434-463Table 43Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|------------|-----------------|----------|--------------------------|------|
| | | | | SYFPEITHI | NIH |
| 439-448 | VLYPVPLESY | 377 | A0201 | 20 | <5 |
| | | | A1 | 21 | 5 |
| | | | A26 | 25 | N/A |
| | | | A3 | 25 | 67.5 |
| 440-448 | LYPVPLESY | 378 | A1 | 16 | <5 |
| 446-455 | ESYEDIHGTL | 379 | A26 | 16 | N/A |
| 448-457 | YEDIHGTLHL | 380 | A1 | 18 | <5 |
| 449-457 | EDIHGTLHL | 381 | B2705 | 15 | <5 |
| 451-460 | IHGTLHLERL | 382 | A0201 | 16 | <5 |

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† Scores are given from the two binding prediction programs referenced above (see example 3). See also figure 46.

Example 44: PRAME 452-480Table 44Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|----------------|-----------------|----------|--------------------------|---------|
| | | | | SYFPEITH I | NIH |
| 454-463 | TLHLERLAYL | 383 | A0201 | 26 | 270.234 |
| | | | A26 | 21 | N/A |
| 455-463 | LHLERLAYL | 384 | A0201 | 22 | <5 |
| | | | B08 | 20 | <5 |
| | | | B1510 | 21 | N/A |
| | | | B2705 | 15 | <5 |
| 456-463 | HLERLAYL | 385 | B08 | 17 | <5 |
| 456-465 | HLERLAYLH A | 386 | A3 | 16 | <5 |
| | | | A1 | 17 | <5 |
| 458-467 | ERLAYLHARL | 387 | A26 | 16 | N/A |
| 459-467 | RLAYLHARL | 388 | A0201 | 24 | 21.362 |
| | | | B08 | 17 | <5 |
| | | | B2705 | 18 | 90 |
| | | | B2709 | 15 | N/A |
| 459-468 | RLAYLHARL R | 389 | A3 | 22 | <5 |
| 460-467 | LAYLHARL | 390 | B08 | 15 | <5 |
| | | | B5101 | 20 | N/A |
| 460-468 | LAYLHARLR | 391 | B5101 | 18 | <5 |
| 461-470 | AYLHARLREL | 392 | A0201 | 20 | <5 |
| | | | B4402 | 16 | N/A |
| 462-470 | YLHARLREL | 393 | A0201 | 28 | 45.203 |
| | | | B08 | 25 | 8 |
| 462-471 | YLHARLRELL | 394 | A0201 | 22 | 48.151 |
| | | | A26 | 16 | N/A |
| 463-471 | LHARLRELL | 395 | A0201 | 15 | <5 |
| | | | B1510 | 22 | N/A |
| 464-471 | HARLRELL | 396 | B08 | 30 | 320 |
| | | | B5101 | 17 | N/A |
| 464-472 | HARLRELLC | 397 | B08 | 20 | 16 |
| 469-478 | ELLCELGRPS | 398 | A3 | 15 | <5 |
| 470-478 | LLCELGRPS | 399 | A0201 | 15 | <5 |

†Scores are given from the two binding prediction programs referenced above (see example 3). See also figure 47.

Example 45: PSA 143-169Table 45Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|------------|-----------------|----------|--------------------------|-----|
| | | | | SYFPEITHI | NIH |
| 144-153 | QEPALGTTCY | 400 | A1 | 15 | <5 |
| 145-153 | EPALGTTCY | 401 | A1 | 17 | <5 |
| | | | A26 | 17 | N/A |

†Scores are given from the two binding prediction programs referenced above (see example 3). See also figure 48.

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Example 46: PSA 156-1883Table 46Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|------------|-----------------|----------|--------------------------|--------|
| | | | | SYFPEITHI | NIH |
| 162-171 | PEEFLTPKKL | 402 | B4402 | 24 | N.A. |
| 163-171 | EEFLTPKKL | 403 | A26 | 17 | N.A. |
| | | | B4402 | 29 | N.A. |
| 165-173 | FLTPKKLQC | 404 | A3 | 20 | <5 |
| | | | B08 | 17 | <5 |
| 165-174 | FLTPKKLQCV | 405 | A0201 | 26 | 735.86 |
| | | | A26 | 15 | N.A. |
| 166-174 | LTPKKLQCV | 406 | A0201 | 21 | <5 |
| | | | A26 | 18 | N.A. |
| 167-174 | TPKKLQCV | 407 | B08 | 16 | <5 |
| | | | B5101 | 22 | N.A. |
| 167-175 | TPKKLQCVD | 408 | B5101 | 15 | <5 |
| 170-179 | KLQCVDLHVI | 409 | A0201 | 24 | 34.433 |
| | | | A3 | 17 | <5 |
| 171-179 | LQCVDLHVI | 410 | A0201 | 15 | <5 |
| | | | B5101 | 16 | 6.292 |

†Scores are given from the two binding prediction programs referenced above (see example 3). See also figure 49.

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Example 47: PSCA 67-94

Table 47

Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|----------------|-----------------|----------|--------------------------|--------|
| | | | | SYFPEITHI | NIH |
| 73-81 | DSQDYVVGK | 411 | A3 | 15 | <5 |
| 74-82 | SQDYVVGKK | 412 | A1 | 16 | <5 |
| 74-83 | SQDYVVGKK N | 413 | A1 | 15 | <5 |
| 76-84 | DYVVGKKNI | 414 | B5101 | 19 | 23.426 |
| 77-84 | YVVGKKNI | 415 | B08 | 16 | <5 |
| 78-86 | YVVGKKNITC | 416 | A3 | 15 | <5 |
| 78-87 | YVVGKKNITCC | 417 | A26 | 15 | N/A |

5 †Scores are given from the two binding prediction programs referenced above (see example 3). See also figure 50.

Example 48: PSMA 378-405

Table 48

10 Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|------------|-----------------|----------|--------------------------|-------|
| | | | | SYFPEITHI | NIH |
| 381-390 | WVFGGIDPQS | 418 | A26 | 16 | N/A |
| | | | A3 | 15 | <5 |
| 385-394 | GIDPQSGAAV | 419 | A0201 | 24 | <5 |
| | | | A0203 | 17 | N/A |
| | | | A1 | 15 | 10 |
| | | | A26 | 15 | N/A |
| | | | A3 | 18 | <5 |
| 386-394 | IDPQSGAAV | 420 | A0201 | 15 | <5 |
| 387-394 | DPQSGAAV | 421 | B5101 | 22 | N/A |
| 387-395 | DPQSGAAVV | 422 | B0702 | 18 | N/A |
| | | | B5101 | 26 | 440 |
| 387-396 | DPQSGAAVVH | 423 | A3 | 15 | <5 |
| 388-396 | PQSGAAVVH | 424 | A3 | 17 | <5 |
| 389-398 | QSGAAVVHEI | 425 | A0201 | 15 | <5 |
| 390-398 | SGAAVVHEI | 426 | A0201 | 19 | <5 |
| | | | B5101 | 21 | 88 |
| 391-398 | GAAVVHEI | 427 | B5101 | 23 | N/A |
| 391-399 | GAAVVHEIV | 428 | A0201 | 17 | <5 |
| | | | B5101 | 20 | 133.1 |
| 392-399 | AAVVHEIV | 429 | B5101 | 19 | N/A |

†Scores are given from the two binding prediction programs referenced above (see example 3). See also figure 51.

Example 49: PSMA 597-623Table 49Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|----------------|-----------------|----------|--------------------------|------|
| | | | | SYFPEITHI | NIH |
| 597-605 | CRDYAVVLR | 430 | B2705 | 22 | N/A |
| 598-607 | RDYAVVLRK Y | 431 | A1 | 17 | <5 |
| | | | A26 | 15 | N/A |
| | | | A3 | 16 | <5 |
| 599-607 | DYAVVLRKY | 432 | A1 | 19 | <5 |
| | | | A26 | 22 | N/A |
| 600-607 | YAVVLRKY | 433 | B5101 | 17 | N/A |
| 602-611 | VVLRKYADKI | 434 | A0201 | 17 | <5 |
| | | | A3 | 18 | <5 |
| 603-611 | VLRKYADKI | 435 | A0201 | 22 | <5 |
| | | | A3 | 16 | <5 |
| | | | B08 | 19 | <5 |
| | | | B5101 | 16 | 5.72 |
| 603-612 | VLRKYADKIY | 436 | A1 | 17 | <5 |
| | | | A26 | 19 | N/A |
| | | | A3 | 19 | <5 |
| 604-611 | LRKYADKI | 437 | B08 | 17 | <5 |
| 604-612 | LRKYADKIY | 438 | A1 | 15 | <5 |
| | | | B2705 | 19 | N/A |
| 605-614 | RKYADKIYSI | 439 | A0201 | 16 | <5 |
| 606-614 | KYADKIYSI | 440 | A0201 | 20 | <5 |
| | | | B08 | 17 | <5 |
| 607-614 | YADKIYSI | 441 | B5101 | 27 | N/A |

†Scores are given from the two binding prediction programs referenced above (see example 3). See also figure 52.

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Example 50: PSMA 615-642Table 50Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|----------------|-----------------|----------|--------------------------|-----|
| | | | | SYFPEITHI | NIH |
| 616-625 | MKHPQEMKT Y | 442 | A1 | 19 | <5 |
| | | | A26 | 16 | N/A |
| 617-625 | KHPQEMKTY | 443 | A1 | 15 | <5 |
| | | | A26 | 16 | N/A |
| 618-627 | HPQEMKTYSV | 444 | A0201 | 15 | <5 |
| | | | B0702 | 17 | N/A |

†Scores are given from the two binding prediction programs referenced above (see example 3). See also figure 53.

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Example 51: SCP-1 57-86Table 51Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|------------|-----------------|----------|--------------------------|---------|
| | | | | SYFPEITHI | NIH |
| 62-71 | IDSDPALQKV | 445 | A0201 | 19 | <5 |
| 63-71 | DSDPALQKV | 446 | A0201 | 17 | <5 |
| | | | A1 | 20 | 7.5 |
| | | | A26 | 15 | N/A |
| | | | B5101 | 15 | 5.324 |
| 67-76 | ALQKVNFLPV | 447 | A0201 | 23 | 132.149 |
| | | | A3 | 16 | <5 |
| 70-78 | KVNFLPVLE | 448 | A3 | 18 | <5 |
| 71-80 | VNFLPVLEQV | 449 | A0201 | 16 | <5 |
| 72-80 | NFLPVLEQV | 450 | A0201 | 18 | <5 |
| 75-84 | PVLEQVGNSD | 451 | A3 | 18 | <5 |
| 76-84 | VLEQVGNSD | 452 | A1 | 15 | <5 |
| | | | A3 | 16 | <5 |

†Scores are given from the two binding prediction programs referenced above (see example 3). See also figure 54.

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Example 52: SCP-1 201-227Table 52Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|------------|-----------------|----------|--------------------------|-----|
| | | | | SYFPEITHI | NIH |
| 202-210 | YEREETRQV | 453 | A0201 | 16 | <5 |
| 202-211 | YEREETRQVY | 454 | A1 | 19 | <5 |
| | | | A3 | 15 | <5 |
| | | | A4402 | 22 | N/A |
| 203-211 | EREETRQVY | 455 | A1 | 27 | <5 |
| | | | A26 | 19 | N/A |
| | | | B2705 | 20 | N/A |
| 203-212 | EREETRQVYM | 456 | A26 | 17 | N/A |
| 204-212 | REETRQVYM | 457 | B2705 | 15 | N/A |
| 211-220 | YMDLNSNIEK | 458 | A1 | 17 | 25 |
| 213-221 | DLNSNIEKM | 459 | A0201 | 20 | <5 |
| | | | A26 | 28 | N/A |
| 216-226 | SNIEKMITAF | 460 | A26 | 19 | N/A |
| | | | B4402 | 19 | N/A |
| 217-225 | NIEKMITAF | 461 | A26 | 26 | N/A |
| | | | B2705 | 17 | N/A |
| | | | B4402 | 16 | N/A |
| 218-225 | IEKMITAF | 462 | B08 | 17 | <5 |

†Scores are given from the two binding prediction programs referenced above (see example 3). See also figure 55.

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Example 53: SCP-1 395-424Table 53Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|------------|-----------------|----------|--------------------------|--------|
| | | | | SYFPEITHI | NIH |
| 397-406 | RLENYEDQLI | 463 | A0201 | 17 | <5 |
| | | | A3 | 15 | <5 |
| 398-406 | LENYEDQLI | 464 | B4402 | 19 | N/A |
| 398-407 | LENYEDQLII | 465 | B4402 | 19 | N/A |
| 399-407 | ENYEDQLII | 466 | B5101 | 17 | 19.36 |
| 399-408 | ENYEDQLIIL | 467 | A26 | 20 | N/A |
| 400-408 | NYEDQLIIL | 468 | A1 | 16 | <5 |
| 400-409 | NYEDQLIILT | 469 | A1 | 16 | <5 |
| | | | A1 | 18 | <5 |
| 401-409 | YEDQLIILT | 470 | B4402 | 16 | N/A |
| | | | A1 | 18 | <5 |
| 401-410 | YEDQLIILTM | 471 | B4402 | 16 | N/A |
| | | | A26 | 18 | N/A |
| 402-410 | EDQLIILTM | 472 | B2705 | 15 | <5 |
| | | | A0201 | 22 | 14.824 |
| 406-415 | IILTMELQKT | 473 | A26 | 16 | N/A |
| 407-415 | ILTMELQKT | 474 | A0201 | 21 | 29.137 |

†Scores are given from the two binding prediction programs referenced above (see example 3).. See also figure 56.

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Example 54: SCP-1 416-442Table 54Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|------------|-----------------|----------|--------------------------|--------|
| | | | | SYFPEITHI | NIH |
| 424-432 | KLTNNKEVE | 475 | A3 | 18 | <5 |
| 424-433 | KLTNNKEVEL | 476 | A0201 | 24 | 74.768 |
| | | | A26 | 18 | N/A |
| | | | A3 | 18 | <5 |
| 425-433 | LTNNKEVEL | 477 | A0201 | 22 | <5 |
| | | | A26 | 21 | N/A |
| | | | B08 | 22 | <5 |
| 429-438 | KEVELEELKK | 478 | A3 | 17 | <5 |
| 430-438 | EVELEELKK | 479 | A1 | 18 | 90 |
| | | | A26 | 17 | N/A |
| | | | A3 | 24 | <5 |
| | | | B2705 | 15 | <5 |
| 430-439 | EVELEELKKV | 480 | A0201 | 15 | <5 |
| | | | A26 | 21 | N/A |
| 431-439 | VELEELKKV | 481 | A0201 | 20 | 80.217 |
| | | | A4402 | 15 | N/A |
| | | | B5101 | 17 | <5 |

†Scores are given from the two binding prediction programs referenced above (see example 3). See also figure 57.

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Example 55: SCP-1 518-545Table 55Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|------------|-----------------|----------|--------------------------|-----|
| | | | | SYFPEITHI | NIH |
| 530-539 | ETSDMTLELK | 482 | A26 | 21 | N/A |
| 531-539 | TSDMTLELK | 483 | A1 | 16 | 15 |

5 †Scores are given from the two binding prediction programs referenced above (see example 3). See also figure 58.

Example 56: SCP-1 545-578Table 5610 Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|------------|-----------------|----------|--------------------------|--------|
| | | | | SYFPEITHI | NIH |
| 548-556 | NKKQEERML | 484 | B08 | 20 | <5 |
| 553-562 | ERMLTQIENL | 485 | A26 | 19 | N/A |
| | | | B4402 | 17 | N/A |
| 554-562 | RMLTQIENL | 486 | A0201 | 24 | 64.335 |
| | | | B2705 | 21 | 150 |
| | | | B2709 | 17 | N/A |
| | | | B4402 | 15 | N/A |
| 555-562 | MLTQIENL | 487 | B08 | 16 | <5 |
| 555-564 | MLTQIENLQE | 488 | A3 | 16 | <5 |
| 560-569 | ENLQETETQL | 489 | A26 | 16 | N/A |
| 561-569 | NLQETETQL | 490 | A0201 | 22 | 87.586 |
| | | | A26 | 19 | N/A |
| | | | A3 | 15 | <5 |
| | | | B08 | 18 | <5 |
| 561-570 | NLQETETQLR | 491 | A3 | 15 | 6 |

†Scores are given from the two binding prediction programs referenced above (see example 3).. See also figure 59.

Example 57: SCP-1 559-585Table 57Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|------------|-----------------|----------|--------------------------|---------|
| | | | | SYFPEITHI | NIH |
| 567-576 | TQLRNELEYV | 492 | A0201 | 16 | 161.729 |
| 568-576 | QLRNELEYV | 493 | A0201 | 24 | 32.765 |
| | | | A3 | 16 | <5 |
| 571-580 | NELEYVREEL | 494 | A0201 | 16 | <5 |
| | | | B4402 | 23 | N/A |
| 572-580 | ELEYVREEL | 495 | A0201 | 17 | <5 |
| | | | A26 | 23 | N/A |
| | | | B08 | 20 | <5 |
| 573-580 | LEYVREEL | 496 | B08 | 19 | <5 |
| 574-583 | EYVREELKQK | 497 | A3 | 16 | <5 |
| 575-583 | YVREELKQK | 498 | A26 | 17 | N/A |
| | | | A3 | 27 | <5 |

†Scores are given from the two binding prediction programs referenced above (see example 3). See also figure 60.

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Example 58: SCP-1 665-701Table 58Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|----------------|-----------------|----------|--------------------------|--------|
| | | | | SYFPEITHI | NIH |
| 675-684 | LLEEVEKAK V | 499 | A0201 | 27 | 31.026 |
| 676-684 | LEEVEKAKV | 500 | A0201 | 15 | <5 |
| 676-685 | LEEVEKAKVI | 501 | A4402 | 22 | N/A |
| 677-685 | EEVEKAKVI | 502 | B08 | 21 | <5 |
| | | | B4402 | 24 | N/A |
| | | | B5101 | 18 | <5 |
| 681-690 | KAKVIAD V | 503 | A0201 | 15 | <5 |
| 683-692 | KVIAD L | 504 | A0201 | 21 | 6.542 |
| | | | A26 | 22 | N/A |
| | | | A3 | 25 | <5 |
| | | | B4402 | 17 | N/A |
| 684-692 | VIAD KL | 505 | A0201 | 26 | 20.473 |
| | | | A26 | 22 | N/A |
| | | | A3 | 17 | <5 |
| | | | B08 | 16 | <5 |
| | | | B2705 | 15 | N/A |
| 685-692 | IAD KL | 506 | B08 | 17 | <5 |
| | | | B5101 | 21 | N/A |

†Scores are given from the two binding prediction programs referenced above (see example 3). See also figure 61.

10

Example 59: SCP-1 694-7205 Table 59Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|-----------------------|-----------------|----------|--------------------------|-----|
| | | | | SYFPEITHI | NIH |
| 694-702 | KEIDKRCQH | 507 | A3 | 16 | <5 |
| | | | A4402 | 17 | N/A |
| 694-703 | KEIDKRCQH K | 508 | A3 | 17 | <5 |
| | | | B4402 | 15 | N/A |
| 695-703 | EIDKRCQHK | 509 | A26 | 20 | N/A |
| | | | A3 | 20 | <5 |
| 695-704 | EIDKRCQH KI | 510 | A0201 | 16 | <5 |
| | | | A26 | 19 | N/A |
| 696-704 | IDKRCQH KI | 511 | B08 | 17 | <5 |
| 697-704 | DKRCQH KI | 512 | B5101 | 16 | N/A |
| 698-706 | KRCQH K I A E | 513 | B2705 | 16 | 60 |
| 698-707 | KRCQH K I A E M | 514 | A26 | 15 | N/A |
| 699-707 | RCQH K I A E M | 515 | A26 | 15 | N/A |
| | | | B2705 | 18 | 9 |
| 701-710 | QH K I A E M V A L | 516 | A26 | 15 | N/A |
| 702-710 | H K I A E M V A L | 517 | A0201 | 15 | <5 |
| | | | A26 | 16 | N/A |
| | | | B4402 | 16 | N/A |
| 703-710 | K I A E M V A L | 518 | B08 | 16 | <5 |

†Scores are given from the two binding prediction programs referenced

[0386] above (see example 3)

10 [0387] See also figure 62.

Example 60: SCP-1 735-769Table 60Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|----------------|-----------------|----------|--------------------------|-------|
| | | | | SYFPEITHI | NIH |
| 737-746 | QEQSSLRASL | 519 | B4402 | 21 | N.A. |
| 738-746 | EQSSLRASL | 520 | A26 | 22 | N.A. |
| | | | B0702 | 15 | 6 |
| 739-746 | QSSLRASL | 521 | B08 | 19 | <5 |
| 741-750 | SLRASLEIEL | 522 | A0201 | 24 | <5 |
| | | | A26 | 17 | N.A. |
| | | | A3 | 16 | <5 |
| 742-750 | LRASLEIEL | 523 | A0201 | 17 | <5 |
| | | | B2705 | 23 | 2000 |
| | | | B2709 | 21 | N.A. |
| 743-750 | RASLEIEL | 524 | B5101 | 17 | N.A. |
| 744-753 | ASLEIELSNL | 525 | A0201 | 20 | <5 |
| | | | A26 | 16 | N.A. |
| 745-753 | SLEIELSNL | 526 | A0201 | 25 | <5 |
| | | | A26 | 22 | N.A. |
| | | | A3 | 15 | <5 |
| | | | B08 | 18 | <5 |
| 745-754 | SLEIELSNLK | 527 | A1 | 15 | 18 |
| | | | A3 | 22 | 20 |
| 746-754 | LEIELSNLK | 528 | B2705 | 16 | 30 |
| | | | B4402 | 15 | N.A. |
| 747-755 | EIELSNLKA | 529 | A1 | 19 | <5 |
| | | | A26 | 18 | N.A. |
| 749-758 | ELSNLKAELL | 530 | A0201 | 17 | <5 |
| | | | A26 | 22 | N.A. |
| 750-758 | LSNLKAELL | 531 | B08 | 21 | <5 |
| 751-760 | SNLKAELLSV | 532 | A0201 | 21 | <5 |
| 752-760 | NLKAELLSV | 533 | A0201 | 26 | 5.599 |
| | | | A3 | 18 | <5 |
| | | | B08 | 16 | <5 |
| 752-761 | NLKAELLSV K | 534 | A3 | 30 | 30 |
| 753-761 | LKAELLSVK | 535 | A3 | 19 | <5 |
| 753-762 | LKAELLSVK K | 536 | A3 | 16 | <5 |
| | | | A3 | 18 | <5 |
| 754-762 | KAELLSVKK | 537 | B2705 | 18 | 30 |
| | | | B4402 | 19 | N.A. |
| 755-763 | AELLSVKKQ | 538 | B4402 | 19 | N.A. |

†Scores are given from the two binding prediction programs referenced above (see example 3). See also figure 63.

Example 61: SCP-1 786-8165 Table 61Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|----------------|-----------------|----------|--------------------------|-------|
| | | | | SYFPEITHI | NIH |
| 787-796 | EKDKKTQT F | 539 | A26 | 19 | N/A |
| | | | B4402 | 15 | N/A |
| 788-796 | KKDKKTQTF | 540 | B08 | 16 | <5 |
| | | | B2705 | 16 | <5 |
| 789-796 | KDKKTQTF | 541 | B08 | 16 | <5 |
| 797-806 | LLETPDIYW K | 542 | A0201 | 16 | <5 |
| | | | A3 | 21 | 90 |
| 798-806 | LETPDIYWK | 543 | B2705 | 15 | 30 |
| | | | B4402 | 16 | N/A |
| 798-807 | LETPDIYWK L | 544 | A0201 | 15 | 7.944 |
| | | | A26 | 15 | N/A |
| | | | A4402 | 24 | N/A |
| 799-807 | ETPDYWKL | 545 | A26 | 31 | N/A |
| | | | B4402 | 16 | N/A |
| 800-807 | TPDIYWKL | 546 | B08 | 16 | <5 |
| | | | B5101 | 19 | N/A |

†Scores are given from the two binding prediction programs referenced

[0390] above (see example 3)

10 [0391] See also figure 64.

Example 62: SCP-1 806-833Table 62Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|------------|-----------------|----------|--------------------------|--------|
| | | | | SYFPEITHI | NIH |
| 809-817 | SKAVPSQTV | 547 | A0201 | 17 | <5 |
| 810-817 | KAVPSQTV | 548 | B5101 | 19 | N/A |
| 812-821 | VPSQTVSRNF | 549 | B0702 | 18 | N/A |
| 815-824 | QTVSRNFTSV | 550 | A0201 | 16 | <5 |
| | | | A26 | 16 | N/A |
| 816-824 | TVSRNFTSV | 551 | A0201 | 16 | 11.426 |
| | | | A26 | 15 | N/A |
| | | | A3 | 16 | <5 |
| 816-825 | TVSRNFTSVD | 552 | A3 | 20 | <5 |
| 823-832 | SVDHGISKDK | 553 | A3 | 21 | <5 |

†Scores are given from the two binding prediction programs referenced above (see example 3). See also figure 65.

5

Example 63: SCP-1 826-853Table 63Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|-------------|-----------------|----------|--------------------------|---------|
| | | | | SYFPEITHI | NIH |
| 829-838 | SKDKRDYLWT | 554 | A1 | 18 | <5 |
| 832-840 | KRDYLWTS A | 555 | B2705 | 16 | 600 |
| 832-841 | KRDYLWTS AK | 556 | A3 | 17 | <5 |
| 833-841 | RDYLWTS AK | 557 | A3 | 23 | <5 |
| | | | B2705 | 18 | 15 |
| 835-843 | YLWTS AKNT | 558 | A0201 | 16 | 284.517 |
| 835-844 | YLWTS AKNTL | 559 | A0201 | 26 | 815.616 |
| | | | A26 | 16 | N/A |
| 837-844 | WTS AKNTL | 560 | B08 | 20 | <5 |
| 841-850 | KNTLSTPLPK | 561 | A3 | 18 | <5 |
| 842-850 | NTLSTPLPK | 562 | A3 | 16 | <5 |

†Scores are given from the two binding prediction programs referenced above (see example 3). See also figure 66.

10

Example 64: SCP-1 832-859Table 64Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|----------------|-----------------|----------|--------------------------|---------|
| | | | | SYFPEITHI | NIH |
| 832-840 | KRDYLWTSA | 563 | B2705 | 16 | 600 |
| 832-841 | KRDYLWTSA K | 564 | A3 | 17 | <5 |
| 833-841 | RDYLWTS AK | 565 | A3 | 23 | <5 |
| | | | B2705 | 18 | 15 |
| 835-843 | YLWTS AKNT | 566 | A0201 | 16 | 284.517 |
| 839-846 | SAKNTLST | 567 | B08 | 16 | <5 |
| 841-850 | KNTLSTPLPK | 568 | A3 | 18 | <5 |
| 842-850 | NTLSTPLPK | 569 | A3 | 16 | <5 |
| 843-852 | TLSTPLPKAY | 570 | A1 | 16 | <5 |
| | | | A26 | 19 | N/A |
| | | | A3 | 18 | <5 |
| | | | B4402 | 17 | N/A |
| 844-852 | LSTPLPKAY | 571 | A1 | 23 | 7.5 |
| | | | A4402 | 18 | N/A |

† Scores are given from the two binding prediction programs referenced above (see example 3). See also figure 67.

5

Example 65: SSX-2 1-27Table 65Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|------------|-----------------|----------|--------------------------|--------|
| | | | | SYFPEITHI | NIH |
| 5-12 | DAFARRPT | 572 | B5101 | 18 | N/A |
| 7-15 | FARRPTVGA | 573 | A0201 | 15 | <5 |
| 8-17 | ARRPTVGAQI | 574 | A3 | 18 | <5 |
| 9-17 | RRPTVGAQI | 575 | B2705 | 23 | 1800 |
| | | | B2709 | 23 | N/A |
| 10-17 | RPTVGAQI | 576 | B5101 | 20 | N/A |
| 13-21 | VGAQIPEKI | 577 | B5101 | 20 | 125.84 |
| 14-21 | GAQIPEKI | 578 | B5101 | 25 | N/A |
| 15-24 | AQIPEKIQKA | 579 | A0201 | 16 | <5 |
| 16-24 | QIPEKIQKA | 580 | A0201 | 21 | 6.442 |
| | | | A26 | 20 | N/A |
| | | | B08 | 17 | <5 |
| 16-25 | QIPEKIQKAF | 581 | A26 | 24 | N/A |
| | | | A3 | 16 | <5 |
| 17-24 | IPEKIQKA | 582 | B5101 | 19 | N/A |
| 17-25 | IPEKIQKAF | 583 | B0702 | 19 | N/A |
| | | | B08 | 15 | <5 |
| | | | B2705 | 16 | <5 |
| 18-25 | PEKIQKAF | 584 | B08 | 16 | <5 |

† Scores are given from the two binding prediction programs referenced above (see example 3). See also figure 68.

10

Example 66: Survivin 116-142Table 66Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|------------|-----------------|----------|--------------------------|--------|
| | | | | SYFPEITHI | NIH |
| 116-124 | ETNNKKKEF | 585 | A26 | 28 | N/A |
| | | | B08 | 20 | <5 |
| 117-124 | TNNKKKEF | 586 | B08 | 16 | <5 |
| 122-131 | KEFEETAKKV | 587 | A0201 | 15 | 71.806 |
| 123-131 | EFEETAKKV | 588 | A26 | 15 | N/A |
| | | | B5101 | 15 | 5.324 |
| 127-134 | TAKKVRRA | 589 | B5101 | 17 | N/A |
| 126-134 | ETAKKVRRA | 590 | A26 | 24 | N/A |
| 128-136 | AKKVRRAIE | 591 | B08 | 19 | <5 |
| 129-138 | KKVRRAIEQL | 592 | A0201 | 15 | <5 |
| 130-138 | KVRRAIEQL | 593 | A0201 | 19 | <5 |
| | | | A26 | 23 | N/A |
| | | | A3 | 22 | <5 |
| | | | B08 | 17 | <5 |
| | | | B2705 | 16 | 30 |
| 130-139 | KVRRAIEQLA | 594 | A3 | 19 | <5 |
| 131-138 | VRRRAIEQL | 595 | B08 | 17 | <5 |

†Scores are given from the two binding prediction programs referenced above (see example 3). See also figure 69.

5

Example 67: BAGE 1-35Table 67Preferred Epitopes Revealed by Housekeeping Proteasome Digestion

| Epitope | Sequence | Sequence ID No. | HLA type | HLA binding predictions† | |
|---------|------------|-----------------|----------|--------------------------|---------|
| | | | | SYFPEITHI | NIH |
| 24-31 | SPVVSRL | 596 | B08 | 19 | <5 |
| | | | B5101 | 17 | N/A |
| 21-29 | KEESPVSW | 597 | B4402 | 23 | N/A |
| 19-27 | LMKEESPVV | 598 | A0201 | 22 | 5.024 |
| | | | B5101 | 15 | <5 |
| 18-27 | RLMKEESPVV | 599 | A0201 | 22 | 105.51 |
| | | | A3 | 18 | <5 |
| 18-26 | RLMKEESPV | 600 | A0201 | 21 | 257.342 |
| | | | A3 | 17 | <5 |
| 14-22 | LLQARLMKE | 601 | A0201 | 18 | <5 |
| | | | A3 | 15 | <5 |
| 13-22 | QLLQARLMKE | 602 | A0201 | 18 | <5 |
| | | | A26 | 15 | N/A |
| | | | A3 | 15 | <5 |

†Scores are given from the two binding prediction programs referenced above (see example 3). See also figure 70.

10

Example 68Epitope Clusters.

Known and predicted epitopes are generally not evenly distributed across the sequences of protein antigens. As referred to above, we have defined segments of sequence containing a higher than average density of (known or predicted) epitopes as epitope clusters. Among the uses of epitope clusters is the incorporation of their sequence into substrate peptides used in proteasomal digestion analysis as described herein, or to otherwise inform the selection and design of such substrates. Epitope clusters can also be useful as vaccine components. Fuller discussions of the definition and uses of epitope clusters is found in PCT Publication No. WO 01/82963; PCT Publication No. WO 03/057823; and U.S. Patent Application No. 09/561,571 entitled EPITOPE CLUSTERS and in U.S. Patent Application No. 10/026,066 entitled "EPITOPE SYNCHRONIZATION IN ANTIGEN PRESENTING CELLS." Epitopes and epitope clusters for many of the TAA mentioned herein have been previously disclosed in PCT Publication No. WO 02/081646; in Patent Application No. 09/561,571; in U.S. Patent Application No. 10/117,937; U.S. Provisional Application Nos. 60/337,017 filed on November 7, 2001, and 60/363,210 filed on March 7, 2002, all entitled EPITOPE SEQUENCES. The teachings and embodiments disclosed in said publications and applications are contemplated as supporting principals and embodiments related to and useful in connection with the present invention.

For the TuAAs survivin (SEQ ID NO. 98) and GAGE-1 (SEQ ID NO. 96) the following tables (68-73) present 9-mer epitopes predicted for HLA-A2 binding using both the SYFPEITHI and NIH algorithms and the epitope density of regions of overlapping epitopes, and of epitopes in the whole protein, and the ratio of these two densities. (The ratio must exceed one for there to be a cluster by the above definition; requiring higher values of this ratio reflect preferred embodiments). Individual 9-mers are ranked by score and identified by the position of their first amino in the complete protein sequence. Each potential cluster from a protein is numbered. The range of amino acid positions within the complete sequence that the cluster covers is indicated, as are the rankings of the individual predicted epitopes it is made up of.

Table 68**HLA-A2 Epitope cluster analysis for Survivin (NIH algorithm)**

Length of protein sequence: 142 amino acids

Number of 9-mers: 134

Number of 9-mers with NIH score = 5: 2

| Cluster | AA | Peptide Rank | Start Position | Score | Peptides/AAs | | Ratio |
|---------------|-------|--------------|----------------|-------|--------------|------------|-------|
| | | | | | Cluster | Whole Pro. | |
| 1 | 13-28 | 1 | 13 | 10.26 | 0.125 | 0.014 | 8.875 |
| SEQ ID NO:603 | | 2 | 20 | 4.919 | | | |

Table 69

HLA-A2 Epitope cluster analysis for Survivin (SYFPEITHI algorithm)

Length of protein sequence: 142 amino acids

Number of 9-mers: 134

Number of 9-mers with SYFPEITHI score = 15: 10

| Cluster | AA | Peptide | Start | Score | Peptides/AAs | | Ratio |
|---------------|---------|---------|----------|-------|--------------|------------|-------|
| | | Rank | Position | | Cluster | Whole Pro. | |
| 1 | 13-28 | 5 | 13 | 17 | 0.125 | 0.070 | 1.775 |
| SEQ ID NO:603 | | 4 | 20 | 18 | | | |
| 2 | 79-111 | 8 | 79 | 15 | 0.182 | 0.070 | 2.597 |
| SEQ ID NO:604 | | 9 | 81 | 15 | | | |
| | | 6 | 88 | 17 | | | |
| | | 1 | 96 | 23 | | | |
| | | 7 | 97 | 16 | | | |
| | | 10 | 103 | 15 | | | |
| 3 | 130-141 | 2 | 130 | 19 | 0.167 | 0.070 | 2.381 |
| SEQ ID NO:605 | | 3 | 133 | 19 | | | |

Table 70

HLA-A2 Epitope cluster analysis for GAGE-1 (NIH algorithm)

Length of protein sequence: 138 amino acids

Number of 9-mers: 130

Number of 9-mers with NIH score = 5: 5

| Cluster | AA | Peptide | Start | Score | Peptides/AAs | | Ratio |
|---------------|---------|---------|----------|----------|--------------|------------|-------|
| | | Rank | Position | | Cluster | Whole Pro. | |
| 1 | 116-133 | 1 | 123 | 1999.734 | 0.278 | 0.036 | 7.667 |
| SEQ ID NO:606 | | 2 | 121 | 161.227 | | | |
| | | 3 | 125 | 49.834 | | | |
| | | 4 | 117 | 37.362 | | | |
| | | 5 | 116 | 6.381 | | | |

5

Table 71

HLA-A2 Epitope cluster analysis for GAGE-1 (SYFPEITHI algorithm)

Length of protein sequence: 138 amino acids

Number of 9-mers: 130

Number of 9-mers with SYFPEITHI score = 5: 6

| Cluster | AA | Peptide | Start | Score | Peptides/AAs | | Ratio |
|---------------|---------|---------|----------|-------|--------------|------------|-------|
| | | Rank | Position | | Cluster | Whole Pro. | |
| 1 | 116-133 | 1 | 116 | 22 | 0.333 | 0.043 | 7.667 |
| SEQ ID NO:606 | | 2 | 123 | 22 | | | |
| | | 3 | 125 | 22 | | | |
| | | 4 | 117 | 17 | | | |
| | | 5 | 120 | 16 | | | |
| | | 6 | 121 | 15 | | | |

Table 72

HLA-A2 Epitope cluster analysis for BAGE (NIH algorithm)

Length of protein sequence: 43 amino acids

Number of 9-mers included: 35

Number of 9-mers with NIH score = 5: 4

| Cluster | AA | Peptide Rank | Start Position | Score | Peptides/AAs | | Ratio |
|---------------|-------|--------------|----------------|---------|--------------|------------|-------|
| | | | | | Cluster | Whole Pro. | |
| 1 | 7-17 | 2 | 7 | 98.267 | 0.182 | 0.093 | 1.955 |
| SEQ ID NO:607 | | 3 | 9 | 11.426 | | | |
| 2 | 18-27 | 1 | 18 | 257.342 | 0.200 | 0.093 | 2.151 |
| SEQ ID NO:608 | | 4 | 19 | 5.024 | | | |

5 Table 73

HLA-A2 Epitope cluster analysis for BAGE (SYFPEITHI algorithm)

Length of protein sequence: 43 amino acids

Number of 9-mers included: 35

Number of 9-mers with SYFPEITHI score = 15: 10

| Cluster | AA | Peptide Rank | Start Position | Score | Peptides/AAs | | Ratio |
|---------------|-------|--------------|----------------|-------|--------------|------------|-------|
| | | | | | Cluster | Whole Pro. | |
| 1 | 2-27 | 6 | 2 | 18 | 0.308 | 0.233 | 1.323 |
| SEQ ID NO:609 | | 9 | 6 | 16 | | | |
| | | 1 | 7 | 23 | | | |
| | | 3 | 9 | 21 | | | |
| | | 5 | 11 | 19 | | | |
| | | 7 | 14 | 18 | | | |
| | | 4 | 18 | 21 | | | |
| | | 2 | 19 | 22 | | | |
| 2 | 30-39 | 8 | 30 | 17 | 0.200 | 0.233 | 0.858 |
| SEQ ID NO:610 | | 10 | 31 | 15 | | | |

[0406] The embodiments of the invention are applicable to and contemplate variations in the sequences of the target antigens provided herein, including those disclosed in the various databases that are accessible by the world wide web. Specifically for the specific sequences disclosed herein, variation in sequences can be found by using the provided accession numbers to access information for each antigen.

15 TYROSINASE PROTEIN; SEQ ID NO 2

1 MLLAVLYCLL WSFQTSAGHF PRACVSSKNL MEKECCPPWS GDRSPCGQLS
GRGSCQNILL
61 SNAPLGPQFP FTGVDDRESW PSVFYNRTCQ CSGNFMGFNC GNCKFGFWGP
NCTERRLLVR

121 RNIFDLSAPE KDKFFAYLTL AKHTISSDYV IPIGTYGQMK NGSTPMFNDI
NIYDLFVWMH
181 YYVSM DALLG GSEIWRDIDF AHEAPAFLPW HRLFLLRWEQ EIQKLTGDEN
FTIPYWDWRD
5 241 AEKCDICTDE YMGGQHPTNP NLLSPASFFS SWQIVCSRLE EYN SHQSLCN
GTPEGPIRRN
301 PGNHDKS RTP RLPSSADVEF CLSLTQYESG SMDKAANFSF RNTLEGFASP
LTGIADASQS
361 SMHNALHIYM NGTMSQVQGS ANDPIFLLHH AFVDSIFEQW LRRHRPLQEV
10 YPEANAPIGH
421 NRESYMPVFI PLYRNGDFFI SSKDLGYDYS YLQSDPDPSF QDYIKSYLEQ
ASRIWSWLLG
481 AAMVGAVLTA LLAGLVSLLC RHKRKQLPEE KQPLLMEKED YHSLYQSHL
15 SSX-2 PROTEIN; SEQ ID NO 3
1 MNGDDAFARR PTVGAQIPEK IQKAFDDIAK YFSKEEWEKM KASEKIFYVY
MKRKYEAMTK
61 LGFKATLPPF MCNKRAEDFQ GNDLDNDPNR GNQVERPQMT FGRLQGISP K
20 IMPKKPAEEG
121 NDSEEVPEAS GPQNDGKELC PPGKPTTSEK IHERSGPKRG EHAWTHRLRE
RKQLVIYEEI
181 SDPEEDDE
25 PSMA PROTEIN; SEQ ID NO 4
1 MWNLLHETDS AVATARPRW LCAGALVLAG GFFLLGFLFG WFIKSSNEAT
NITPKHNMKA
61 FLDELKAENI KKFLYNFTQI PHLAGTEQNF QLAKQIQSQW KEFGLDSVEL
30 AHYDVLLSYP
121 NKTHPNYISI INEDGNEIFN TSLFEPPPPG YENVSDIVPP FSAFSPQGM P
EGDLVYVNYA
181 RTEDFFKLER DMKINCSGKI VIARYGKVFR GNKVKNQALA GAKGVILYSD
PADYFAPGVK
35 241 SYPDGWNLP GGVQRGNI LN LGAGDPLTP GYPANEYAYR RGIAEAVGLP
SIPVHPIGYY
301 DAQKLLEKMG GSAPPDSSWR GSLKVPYNVG PGFTGNFSTQ KVKMHIHSTN
EVTRIYNVIG
361 TLRGAVEPDR YVILGGHRDS WVFGGIDPQS GAAVVHEIVR SFGTLKKEGW
40 RPRRTILFAS
421 WDAEEFGLLG STEWAEENS R LLQERG VAYI NADSSIEGNY TLRVDCTPLM
YSLVHNLTKE
481 LKSPDEGFEG KSLYESWTKK SPSPEFSGMP RISKLGSGND FEVFFQRLGI
ASGRARYTKN
45 541 WETNKFSGYP LYHSVYETYE LVEKFYDPMF KYHLTVAQVR GGMVFELANS
IVLPFDCRDY
601 AVVLRKYADK IYSISMKHPQ EMKTYSVSFD SLFSAVKNFT EIASKFSERL
QDFDKSNPIV
661 LRMMNDQLMF LERAFIDPLG LPDRPFYRHV IYAPSSH NKY AGESFPGIYD
50 ALFDIESKVD
721 PSKAWGEVKR QIYVAAFTVQ AAAETLSEVA
Homo sapiens tyrosinase (oculocutaneous albinism IA) (TYR), mRNA.;
55 ACCESSION NM_000372
VERSION NM_000372.1 GI:4507752
SEQ ID NO 2
/translation="MLLAVLYCLLSFQTSAGHFPRACVSSKNLMEKECCPPWSGDRS

PCGQLSGRGSCQNILLSNAPLGPFQFPFTGVDDRESWPSVFYNRTCQCSGNFMGFNCGN
 CKFGFWGPNCTERRLLVRRNIFDLSAPEKDKFFAYLTLAKHTISSDYVIPIGTYGQMK
 5 NGSTPMFNDINIYDLFVWMHYVVSMDALLGGSEIWRDIDFAHEAPAFLPWHRLELLRW
 EQEIQKLTGDENFTIPYWDWRDAEKCDICTDEYMGGQHPTNPNNLLSPASFFSSWQIVC
 10 SRLEEYNHQSCLNGTPEGPLRRNPGNHDKSRTPRLPSSADVEFCLSLTQYESGSMDK
 AANFSFRNTLEGFASPLTGIADASQSSMHNALHIYMNGTMSQVQGSANDPIFLLHHAF
 VDSIFEQWLRRHRPLQEVYPEANAPIGHNRESYMPFFIPLYRNGDFFISSKDLGYDYS
 15 YLQDSDPDSFQDYIKSYLEQASRIWSWLLGAAMVGAVLTALLAGLVSLLCRHKRKQLP
 EEKQPLLMEKEDYHSLYQSHL"

SEQ ID NO 5
 20 ORIGIN
 1 atcactgtag tagtagctgg aaagagaaat ctgtgactcc aattagccag
 ttcctgcaga
 61 ccttgtgagg actagaggaa gaatgctcct ggctgttttg tactgcctgc
 tgtggagttt
 25 121 ccagacctcc gctggccatt tccctagagc ctgtgtctcc tctaagaacc
 tgatggagaa
 181 ggaatgctgt ccaccgtgga gcggggacag gagtccctgt ggccagcttt
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 35 421 agagagacga ctcttgggtga gaagaaacat cttcgatttg agtgccccag
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 781 tccatatttg gactggcggg atgcagaaaa gtgtgacatt tgcacagatg
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 ctgttttcac
 25 1861 tcagcccttt taacattttc ccctaagccc atatgtctaa ggaaaggatg
 ctatttggtg
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30

Homo sapiens synovial sarcoma, X breakpoint 2 (SSX2), mRNA.
 ACCESSION NM_003147
 VERSION NM_003147.1 GI:10337582
 SEQ ID NO 3

35

/translation="MNGDDAFARRPTVGAQIPEKIQKAFDDIAKYFSKEEWEKMKASE
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40

RLQGISPKIMPKKPAEEGNDSEEVPEASGPQNDGKELCPPGKPTTSEKIHERSGPKRG
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SEQ ID NO 6

ORIGIN

45

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cctctgagaa
5      541 gattcacgag agatctggac caaaagggg ggaacatgcc tggaccaca
gactgctga
      601 gagaaaacag ctggtgattt atgaagagat cagcgaccct gaggaagatg
acgagtaact
      661 cccctcaggg atacgacaca tgcccatgat gagaagcaga acgtggtgac
10 ctttcacgaa
      721 catgggcatg gctgcggacc cctcgtcatc aggtgcatag caagtg

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15 Homo sapiens folate hydrolase (prostate-specific membrane antigen)
 1 (FOLH1), mRNA.
 ACCESSION NM_004476
 VERSION NM_004476.1 GI:4758397

20 SEQ ID No. 4
 /translation="MWNLLHETDSAVATARRPRWLCAGALVLAGGFLLGFLFGWFIK
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 25 FGLDSVELAHYDVLLSYPNKTHPNYISIINEDGNEIFNTSLFEPPPPGYENVSDIVPP
 FSAFSPQGMPEGDLVYVNYARTEDFFKLERDMKINCSGKIVARIYRGKVFGRGNKVNAQ
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 30 YAYRRGIAEAVGLPSIPVHPIGYYDAQKLEKMGGSAPPDSSWRGSLKVPYNVGPFT
 GNFSTQKVKMHIHSTNEVTRIYNVIGTLRGAVEPDRYVILGGHRDSWVFGGIDPQSGA
 35 AVVHEIVRSFGTLKKEGWRPRRTILFASWDAEEFGLLGSTEWAEENSRLQERGVAYI
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 40 DPMFKYHLTVAQVRGGMVFELANSIVLPFDCRDYAVVLRKYADKIYSISMKHPQEMKT
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 45 DRPFYRHVIYAPSSHNKYAGESFPGIYDALFDIESKVDPSKAWGEVKRQIYVAAFTVQ
 AAAETLSEVA"

SEQ ID NO 7
 ORIGIN
 50 1 ctcaaaaggg gccgatttc cttctcctgg aggcagatgt tgcctctctc
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 61 attggttcag tgcactctag aaacactgct gtggtggaga aactggaccc
 caggtctgga
 121 gcgaattcca gcctgcaggg ctgataagcg aggcattagt gagattgaga
 55 gagactttac
 181 cccgccgtgg tggttgagg gcgcgcagta gagcagcagc acaggcgagg
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 ggctgtggcc
 301 accgcgcgcc gccgcgcctg gctgtgcgct ggggcgctgg tgctggcggg
 tggcttcttt
 5 361 ctccctcggt tcctcttcgg gtggtttata aaatccctcca atgaagctac
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 421 ccaaagcata atatgaaagc atttttggat gaattgaaag ctgagaacat
 caagaagttc
 481 ttatataatt ttacacagat accacattta gcaggaacag aacaaaactt
 10 tcagcttgca
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 aattaatgaa
 15 661 gatggaaatg agattttcaa cacatcatta tttgaaccac ctccctccagg
 atatgaaaat
 721 gtctcgata ttgtaccacc tttcagtgtt ttctctctc aaggaatgcc
 agagggcgat
 781 ctagtgtatg ttaactatgc acgaactgaa gacttcttta aattggaacg
 20 ggacatgaaa
 841 atcaattgct ctgggaaaat tgtaattgcc agatatggga aagttttcag
 aggaaataag
 901 gttaaaaatg cccagctggc aggggccaaa ggagtcattc tctactccga
 ccttgctgac
 25 961 tactttgctc ctgggggtgaa gtcctatcca gatgggttga atcttctctg
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 1201 ccaccagata gcagctggag aggaagtctc aaagtgccct acaatgttgg
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 35 1261 actggaaact tttctacaca aaaagtcaag atgcacatcc actctaccaa
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 caggataagc
 1801 aaattgggat ctggaaatga ttttgaggtg ttcttccaac gacttggaat
 tgcttcaggc
 55 1861 agagcacggt atactaaaaa ttgggaaaca aacaaattca ggggctatcc
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 1921 agtgtctatg aaacatatga gttggtggaa aagttttatg atccaatgtt
 taaatatcac

25

30

45

| | | | | | | |
|-------------|------------|------------|------------|-------------|-------------|------------|
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| accaaagcct | 121 | ggaacaggca | gctgtatcca | gagtggacag | aagcccagag | acttgactgc |
| tggagagggtg | 181 | gtcaagtgtc | cctcaaggtc | agtaatgatg | ggcctacact | gattggtgca |
| aatgcctcct | 241 | tctctattgc | cttgaacttc | cctggaagcc | aaaagggtatt | gccagatggg |
| caggttatct | 301 | gggtcaacaa | taccatcatc | aatgggagcc | aggtgtgggg | aggacagcca |
| gtgtatcccc | | | | | | |

| | | | | | | |
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| | 361 | aggaaactga | cgatgcctgc | atcttccctg | atggtggacc | ttgcccattct |
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| | 421 | ctcagaagag | aagctttggt | tatgtctgga | agacctgggg | tgagggactc |
| | | ccttctcagc | | | | |
| 5 | 481 | ctatcatcca | cacttgtggt | tacttctttc | tacctgatca | cctttctttt |
| | | ggccgcccct | | | | |
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| 10 | 601 | cttagcacct | agcccccttc | aagctctatc | ataattcttt | ctggcaactc |
| | | ttggcctcaa | | | | |
| | 661 | ttgtagtcct | accccatgga | atgcctcatt | aggaccctt | ccctgtcccc |
| | | ccatatcaca | | | | |
| | 721 | gcottccaaa | caccctcaga | agtaatcata | cttctgacc | tcccatctcc |
| | | agtgccgttt | | | | |
| 15 | 781 | cgaagcctgt | ccctcagtc | cctttgacca | gtaatctctt | cttccttgct |
| | | tttcattcca | | | | |
| | 841 | aaaatgcttc | aggccaatac | tggcaagttc | tagggggccc | agtgtctggg |
| | | ctgagcattg | | | | |
| 20 | 901 | ggacaggcag | ggcaatgctg | ggcacacaca | ccatggaagt | gactgtctac |
| | | catgccggg | | | | |
| | 961 | gatcccgag | ctatgtgcct | cttgctcatt | ccagctcagc | cttcaccatt |
| | | actggttaag | | | | |
| | 1021 | gttcaggaag | ggcaaggcca | gttgtagggc | aaagagaagg | caggagggct |
| | | tggatggact | | | | |
| 25 | 1081 | gcaaaggaga | aaggtgaaat | gctgtgcaaa | cttaaagtag | aagggccagg |
| | | aagacctagg | | | | |
| | 1141 | cagagaaatg | tgaggcttag | tgccagtga | gggccagcca | gtcagcttgg |
| | | agttggaggg | | | | |
| | 1201 | tgtggctgtg | aaaggagaag | ctgtggctca | ggcctgggttc | tcaccttttc |
| 30 | | tggctccaat | | | | |
| | 1261 | cccagaccag | gtgcctttct | ccgtgagcgt | gtcccagttg | cgggccttgg |
| | | atggagggaa | | | | |
| | 1321 | caagcacttc | ctgagaaatc | agcctctgac | ctttgccttc | cagctccatg |
| | | acccagtggt | | | | |
| 35 | 1381 | ctatctggct | gaagctgacc | tctcctacac | ctgggacttt | ggagacagta |
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| | 1441 | gatctctcgg | gcacctgtgg | tcactcatac | ttacctggag | cctggcccag |
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| | 1501 | ggtggtcctg | caggctgcca | ttcctctcac | ctcctgtggc | tcctccccag |
| 40 | | ttccaggcac | | | | |
| | 1561 | cacagatggg | cacaggccaa | ctgcagaggc | ccctaacc | acagctggcc |
| | | aagtgcctac | | | | |
| | 1621 | tacagaagtt | gtgggtacta | cacctggtca | ggcgccaact | gcagagccct |
| | | ctggaaccac | | | | |
| 45 | 1681 | atctgtgcag | gtgccaacca | ctgaagtc | aagcactgca | cctgtgcaga |
| | | tgccaactgc | | | | |
| | 1741 | agagagcaca | ggtatgacac | ctgagaagg | gccagtttca | gaggtcatgg |
| | | gtaccacact | | | | |
| | 1801 | ggcagagatg | tcaactccag | aggctacagg | tatgacacct | gcagagggtat |
| 50 | | caattgtggt | | | | |
| | 1861 | gctttctgga | accacagctg | cacaggtaac | aactacagag | tgggtggaga |
| | | ccacagctag | | | | |
| | 1921 | agagctacct | atccctgagc | ctgaagggtcc | agatgccagc | tcaatcatgt |
| | | ctacggaaag | | | | |
| 55 | 1981 | tattacaggt | tccctgggcc | ccctgctgga | tggtacagcc | accttaaggc |
| | | tgggtgaagag | | | | |
| | 2041 | acaagtcccc | ctggattgtg | ttctgtatcg | atatgggttcc | ttttccgtca |
| | | ccctggacat | | | | |

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tgagattgac
      2761 agaaacacct atatttcccc cagtcttccc tgggagacta ctattaactg
aaataaaa
25      //

```

Homo sapiens kallikrein 3, (prostate specific antigen) (KLK3), mRNA.

```

30  ACCESSION    NM_001648
    VERSION      NM_001648.1  GI:4502172
    SEQ ID NO 78

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35  /translation="MWVPVVFLLSVTWIGAAPLILSRIVGGWECEKHSQPWQVLVAS
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    LRPGDDSSHDLMLRLSEPAELTDAVKVMDLPTQEPALGTTTCYASGWGSIEPEEFLLTPKKLQCVDL
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40  SEQ ID NO 86
    ORIGIN

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45      121 gggaggctgg gagtgcgaga agcattccca accctggcag gtgcttgtgg
cctctcgtgg
      181 cagggcagtc tgccggcggtg ttctggtgca ccccagtggt gtccctcacag
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tgtgtgcgca
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ttcaagggtat
      721 cacgtcatgg ggcagtgaac catgtgccct gcccgaaagg ccttccttgt
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      781 ggtgcattac cggaagtgga tcaaggacac catcgtggcc aaccctgag
cacccctatc
      841 aacccctat tgtagtaaac ttggaacctt ggaaatgacc aggccaagac
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15      901 ccagttctac tgacctttgt ccttaggtgt gaggtccagg gttgctagga
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      1021 ctgggggaata ctggccatgc ctggagacat atcactcaat ttctctgagg
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25      1201 gcacaacgca ccagacactc acagcaagga tggagctgaa aacataacct
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tcctttggca
      1321 tgggatgggg atgaagtaag gagagggact ggacccctg gaagctgatt
30 cactatgggg
      1381 ggaggtgtat tgaagtcctc cagacaacct tcagatttga tgatttccta
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35

```

Human autoimmunogenic cancer/testis antigen NY-ESO-1 mRNA,
complete cds.

ACCESSION U87459

40 VERSION U87459.1 GI:1890098

SEQ ID NO 74

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45      /translation="MQAEGRGTTGGSTGDADGPGPGIPDGPGGNAGGPGEAG
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      YLAMPFATPMEAELARRSLAQDAPPLPVPGVLLKEFTVSGNILTIRLTAADH
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SEQ ID NO 84

ORIGIN

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      121 ttcttgatgg ccaggggggc aatgctggcg gcccaggaga ggcgggtgcc
55 acgggcggca
      181 gaggtccccg gggcgcaggg gcagcaaggg cctcggggcc gggaggaggc
gccccgcggg

```



```

      241 gtccgcatgg cggcgcggct tcagggctga atggatgctg cagatgcggg
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5      361 agctggcccc caggagcctg gcccaggatg ccccaccgct tcccggtgcca
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      481 gccaaactgca gctctccatc agctcctgtc tccagcagct ttccctggtg
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      601 agcctggcgc cccttcctag gtcatgcctc ctcccctagg gaatggtccc
agcacgagtg
15      661 gccagttcat tgtggggggc tgattgtttg tcgctggagg aggacggctt
acatgtttgt
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20 LAGE-1a protein [Homo sapiens].
 ACCESSION CAA11116
 PID g3255959
 VERSION CAA11116.1 GI:3255959

25 SEQ ID NO 75
 ORIGIN

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      1 mqaegrgtgg stgdadgpgg pgipdgpggn aggpgeagat ggrgprgaga
arasgprgga
      61 prgphggaas aqdgrcpcga rrpdsrllle hitmpfsspm eaelvrrils
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35

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LAGE-1b protein [Homo sapiens].
 ACCESSION CAA11117
 PID g3255960
 40 VERSION CAA11117.1 GI:3255960

SEQ ID NO 76
 ORIGIN

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      1 mqaegrgtgg stgdadgpgg pgipdgpggn aggpgeagat ggrgprgaga
45 arasgprgga
      61 prgphggaas aqdgrcpcga rrpdsrllle hitmpfsspm eaelvrrils
rdaaplprpg
      121 avlkdftvsg nllfmsvwdq dregagrmrv vgwglgsasp egqkardlrt
pkhkvsegrp
50      181 gtpgpppppeg aqgdgcrava fnvmfsaphi
//

```

Human antigen (MAGE-1) gene, complete cds.
 55 ACCESSION M77481
 VERSION M77481.1 GI:416114
 SEQ ID NO 71

/translation="MSLEQORSLHCKPEEALDAQQALGLVCVQAATSSSSPL
 VLGTLEEVPTAGSTDPPQSPQGASAFPTTINFTRQRQPSEGSSSREEEGPST
 SCILESLEFRAVITKKVADLVGFLLKLYRAREPVTKAEMLESVIKNYKHCPE
 IFGKASESLQLVFGIDVKEADPTGHSYVLVTCGLGLSYDGLLDGNQIMPKTGF
 LIIVLVMIAMEGGHAPEEEIWEELSVMEVYDGREHSAYGEPKLLTQDLVQE
 KYLEYRQVPDSDPARYEFLWGPRLAETSIVKVLEYVIKVSARVRFFFPRLR
 EAALREEEEGV"

5
 10 SEQ ID NO 81
 ORIGIN
 1 ggatccaggc cctgccagga aaaatataag ggccctgcgt gagaacagag
 ggggtcatcc
 61 actgcatgag agtggggatg tcacagagtc cagcccaccc tcctggtagc
 15 actgagaagc
 121 cagggctgtg cttgcggtct gcaccctgag ggcccgtgga ttctcttcc
 tggagctcca
 181 ggaaccaggc agtgaggcct tggctctgaga cagtatcctc aggtcacaga
 gcagaggatg
 20 241 cacaggggtgt gccagcagtg aatgtttgcc ctgaatgcac accaagggcc
 ccacctgcca
 301 caggacacat aggactccac agagtctggc ctcacctccc tactgtcagt
 cctgtagaat
 361 cgacctctgc tggccggctg taccctgagt accctctcac ttctccttc
 25 aggttttcag
 421 gggacaggcc aaccagagg acaggattcc ctggaggcca cagaggagca
 ccaaggagaa
 481 gatctgtaag taggcctttg ttagagtctc caaggttcag ttctcagctg
 aggcctctca
 30 541 cacactccct ctctcccag gcctgtgggt cttcattgcc cagctcctgc
 ccacactcct
 601 gcctgctgcc ctgacgagag tcatcatgtc tcttgagcag aggagtctgc
 actgcaagcc
 661 tgaggaagcc cttgaggccc aacaagaggc cctgggcctg gtgtgtgtgc
 35 aggctgccac
 721 ctctcctcc tctcctctgg tcctgggcac cctggaggag gtgcccactg
 ctgggtcaac
 781 agatcctccc cagagtcctc agggagcctc cgcctttccc actaccatca
 acttcactcg
 40 841 acagaggcaa ccagtgagg gttccagcag ccgtgaagag gaggggcaa
 gcacctcttg
 901 taccctggag tccttgttcc gagcagtaat cactaagaag gtggctgatt
 tgggtggttt
 961 tctgctcctc aaatatcgag ccaggagacc agtcacaaag gcagaaatgc
 45 tggagagtgt
 1021 catcaaaaat tacaagcact gttttcctga gatcttcggc aaagcctctg
 agtccttgca
 1081 gctggtcttt ggcattgacg tgaaggaagc agacccacc ggccactcct
 atgtccttgt
 50 1141 cacctgccta ggtctctcct atgatggcct gctgggtgat aatcagatca
 tgcccaagac
 1201 aggcttctcg ataattgtcc tggatcatgat tgcaatggag ggcggccatg
 ctcttgagga
 1261 ggaaatctgg gaggagctga gtgtgatgga ggtgtatgat gggaggaggc
 55 acagtgccta
 1321 tggggagccc aggaagctgc tcaccaaga tttggtgcag gaaaagtacc
 tggagtaccg

```

      1381 gcaggtgccg gacagtgatc ccgcacgcta tgagttcctg tgggggtccaa
      gggccctcgc
      1441 tgaaaccagc tatgtgaaag tccttgagta tgtgatcaag gtcagtgcaa
      gagttcgctt
5      1501 tttcttccca tccctgcgtg aagcagcttt gagagaggag gaagagggag
      tctgagcatg
      1561 agttgcagcc aaggccagtg ggagggggac tgggccagtg caccttccag
      ggccgcgtcc
      1621 agcagcttcc cctgcctcgt gtgacatgag gccattctt cactctgaag
10      agagcgggtca
      1681 gtgttctcag tagtaggttt ctgttctatt gggtgacttg gagatttatac
      tttgttctct
      1741 tttggaattg ttcaaagtgt tttttttaag ggatggttga atgaacttca
      gcatccaagt
15      1801 ttatgaatga cagcagtcac acagttctgt gtatatagtt taagggttaag
      agtcttgtgt
      1861 tttattcaga ttgggaaatc cattctatct tgtgaattgg gataataaca
      gcagtggaat
      1921 aagtacttag aaatgtgaaa aatgagcagt aaaatagatg agataaagaa
20      ctaaagaaat
      1981 taagagatag tcaattcttg ccttatacct cagtctattc tgtaaaattt
      ttaaagatat
      2041 atgcatacct ggatttcctt ggcttctttg agaatgtaag agaaattaaa
      tctgaataaa
25      2101 gaattcttcc tgttcactgg ctcttttctt ctccatgcac tgagcatctg
      ctttttggaa
      2161 ggccctgggt tagtagtgga gatgctaagg taagccagac tcatacccac
      ccatagggtc
      2221 gtagagtcta ggagctgcag tcacgtaatc gaggtggcaa gatgtcctct
30      aaagatgtag
      2281 ggaaaagtga gagaggggtg aggggtgtggg gctccgggtg agagtgggtg
      agtgtcaatg
      2341 ccctgagctg gggcattttg ggctttggga aactgcagtt ccttctgggg
      gagctgattg
35      2401 taatgatctt gggtgatcc
      //

```

Human MAGE-2 gene exons 1-4, complete cds.

```

40  ACCESSION   L18920
      VERSION   L18920.1  GI:436180
      SEQ ID NO 72

```

```

45  /translation="MPLEQRSQHCKPEEGLEARGEALGLVGAQAPATEEQQTASSSSTLVEVT
      LGEVPAADSPSPPHSPQGASSFSTTINYTLWRQSDGSSNQEEEGPRMFPDLE
      SEFQAAISRKMVELVHFLLLKYRAREPVTKAEMLESVLRNCQDFFPVI FSKASEYLQLVFGIE
      VVEVVPISHLYILVTCLGLSYDGLLDGNQVMPKTGLLIIVLAI IAIEGDCAPEEKIWEELSML
      EVFEGREDSVFAHPRKLLMQDLVQENYLEYRQVPGSDPACYEFLWGPRALIETSYVKVLHHTL
      KIGGEPHISYPPLHERALREGEE"

```

```

50  SEQ ID NO 82
      ORIGIN

```

```

      1 attccttcat caaacagcca ggagtgagga agaggaccct cctgagtgag
      gactgaggat
      61 ccaccctcac cacatagtgg gaccacagaa tccagctcag cccctcttgt
55      cagccctggg
      121 acacactggc aatgatctca ccccgagcac acccctcccc ccaatgccac
      ttcgggccga

```

| | | | | | | |
|----|------|-------------|-------------|-------------|------------|-------------|
| | 181 | ctcagagtca | gagacttggt | ctgaggggag | cagacacaat | cggcagagga |
| | | tggcgggtcca | | | | |
| | 241 | ggctcagtct | ggcatccaag | tcaggacctt | gagggatgac | caaaggcccc |
| | | tcccaccccc | | | | |
| 5 | 301 | aactcccccg | accccaccag | gatctacagc | ctcaggatcc | ccgtcccaat |
| | | ccctaccctt | | | | |
| | 361 | acaccaacac | catcttcatg | cttaccacca | ccccccatc | cagatcccca |
| | | tccgggcaga | | | | |
| 10 | 421 | atccggttcc | acccttgccg | tgaaccagg | gaagtcacgg | gcccggtatgt |
| | | gacgccactg | | | | |
| | 481 | acttgacacat | tggagggtcag | aggacagcga | gattctcgcc | ctgagcaacg |
| | | gcctgacgtc | | | | |
| | 541 | ggcggaggga | agcaggcgca | ggctccgtga | ggaggcaagg | taagacgccg |
| | | agggaggact | | | | |
| 15 | 601 | gaggcgggcc | tcacccaga | cagagggccc | ccaataatcc | agcgctgcct |
| | | ctgctgccgg | | | | |
| | 661 | gcctggacca | ccctgcaggg | gaagacttct | cagggtcagt | cgccaccacc |
| | | tcaccccgcc | | | | |
| 20 | 721 | acccccgcc | gctttaaccg | cagggaaactc | tggcgtaaga | gctttgtgtg |
| | | accagggcag | | | | |
| | 781 | ggctgggttag | aagtgtctag | ggcccagact | cagccaggaa | tcaagggtcag |
| | | gacccaaga | | | | |
| | 841 | ggggactgag | ggcaaccac | cccctaccct | cactaccaat | cccatcccc |
| | | aacaccaacc | | | | |
| 25 | 901 | ccacccccat | ccctcaaaca | ccaacccac | ccccaaacc | cattcccatc |
| | | tcctcccca | | | | |
| | 961 | ccaccatcct | ggcagaatcc | ggctttgccc | ctgcaatcaa | cccacggaag |
| | | ctccgggaat | | | | |
| 30 | 1021 | ggcggccaag | cacgcggatc | ctgacgttca | catgtacggc | taagggaggg |
| | | aaggggttgg | | | | |
| | 1081 | gtctcgtgag | tatggccttt | gggatgcaga | ggaagggcc | aggcctcctg |
| | | gaagacagtg | | | | |
| | 1141 | gagtccttag | gggaccagc | atgccaggac | agggggccca | ctgtaccctt |
| | | gtctcaaact | | | | |
| 35 | 1201 | gagccacctt | ttcattcagc | cgagggaatc | ctagggatgc | agaccactt |
| | | cagcaggggg | | | | |
| | 1261 | ttggggccca | gcctgcgagg | agtcaagggg | aggaagaaga | gggaggactg |
| | | aggggacctt | | | | |
| 40 | 1321 | ggagtccaga | tcagtggcaa | ccttgggctg | ggggatcctg | ggcacagtgg |
| | | ccgaatgtgc | | | | |
| | 1381 | cccgtgctca | ttgcaccttc | aggggtgacag | agagttgagg | gctgtggtct |
| | | gagggctggg | | | | |
| | 1441 | acttcaggtc | agcagaggga | ggaatcccag | gatctgccgg | acccaagggtg |
| | | tgcccccttc | | | | |
| 45 | 1501 | atgaggactg | gggatacccc | cggcccagaa | agaagggatg | ccacagagtc |
| | | tggaagtccc | | | | |
| | 1561 | ttgttcttag | ctctggggga | acctgatcag | ggatggccct | aagtgacaat |
| | | ctcatttgta | | | | |
| 50 | 1621 | ccacaggcag | gaggttgggg | aaccctcagg | gagataaggt | gttgggtgtaa |
| | | agaggagctg | | | | |
| | 1681 | tctgctcatt | tcagggggtt | gggggttgag | aaagggcagt | ccctggcagg |
| | | agtaaagatg | | | | |
| | 1741 | agtaaccac | aggaggccat | cataacgttc | accctagaac | caaaggggtc |
| | | agccctggac | | | | |
| 55 | 1801 | aacgcacgtg | ggggtaacag | gatgtggccc | ctcctcactt | gtctttccag |
| | | atctcaggga | | | | |
| | 1861 | gttgatgacc | ttgttttcag | aaggtgactc | aggtcaacac | aggggccccca |
| | | tctggtcgac | | | | |

| | | | | | | |
|----|------|-------------|-------------|-------------|------------|-------------|
| | 1921 | agatgcagtg | gttctaggat | ctgccaagca | tccaggtgga | gagcctgagg |
| | | taggattgag | | | | |
| | 1981 | ggtaccctg | ggccagaatg | cagcaagggg | gccccataga | aatctgccct |
| 5 | | gcccctgcgg | | | | |
| | 2041 | ttacttcaga | gaccctgggc | agggctgtca | gctgaagtcc | ctccattatc |
| | | ctgggatctt | | | | |
| | 2101 | tgatgtcagg | gaaggggagg | ccttggtctg | aaggggctgg | agtcagggtca |
| | | gtagaggag | | | | |
| 10 | 2161 | ggtctcaggc | cctgccagga | gtggacgtga | ggaccaagcg | gactcgtcac |
| | | ccaggacacc | | | | |
| | 2221 | tggaactcaa | tgaatttgga | catctctcgt | tgtccttcgc | gggaggacct |
| | | ggtcacgtat | | | | |
| | 2281 | ggccagatgt | gggtcccctc | atatccttct | gtaccatata | agggatgtga |
| | | gttcttgaca | | | | |
| 15 | 2341 | tgagagattc | tcaagccagc | aaaaggggtg | gattaggccc | tacaaggaga |
| | | aaggtgaggg | | | | |
| | 2401 | ccctgagtga | gcacagaggg | gaccctccac | ccaagtagag | tggggacctc |
| | | acggagtctg | | | | |
| | 2461 | gccaaccctg | ctgagacttc | tgggaatccg | tggctgtgct | tgcagtctgc |
| 20 | | acactgaagg | | | | |
| | 2521 | cccgtgcatt | cctctcccag | gaatcaggag | ctccaggaac | caggcagtga |
| | | ggccttggtc | | | | |
| | 2581 | tgagtcagtg | tcctcaggtc | acagagcaga | ggggacgcag | acagtgccaa |
| | | cactgaaggt | | | | |
| 25 | 2641 | ttgcctggaa | tgcacaccaa | gggccccacc | cgcccagAAC | aaatgggact |
| | | ccagagggcc | | | | |
| | 2701 | tggcctcacc | ctccctattc | tcagtctctg | agcctgagca | tgtgctggcc |
| | | ggctgtaccc | | | | |
| | 2761 | tgagggtgcc | tcccacttcc | tccttcagggt | tctgaggggg | acaggctgac |
| 30 | | aagtaggacc | | | | |
| | 2821 | cgaggcactg | gaggagcatt | gaaggagaag | atctgtaagt | aagcctttgt |
| | | cagagcctcc | | | | |
| | 2881 | aaggttcagt | tcagttctca | cctaaggcct | cacacacgct | ccttctctcc |
| | | ccaggcctgt | | | | |
| 35 | 2941 | gggtcttcat | tgccagctc | ctgcccgcac | tcctgcctgc | tgccctgacc |
| | | agagtcatca | | | | |
| | 3001 | tgcctcttga | gcagaggagt | cagcactgca | agcctgaaga | aggccttgag |
| | | gcccagaggag | | | | |
| | 3061 | aggccctggg | cctgggtgggt | gcgcaggctc | ctgctactga | ggagcagcag |
| 40 | | accgcttctt | | | | |
| | 3121 | cctcttctac | tctagtggaa | gttaccctgg | gggaggtgcc | tgctgccgac |
| | | tcaccgagtc | | | | |
| | 3181 | ctccccacag | tcctcaggga | gcctccagct | tctcgactac | catcaactac |
| | | actctttgga | | | | |
| 45 | 3241 | gacaatccga | tgagggctcc | agcaaccaag | aagaggaggg | gccaagaatg |
| | | tttcccgaac | | | | |
| | 3301 | tgaggtccga | gttccaagca | gcaatcagta | ggaagatggg | tgagttgggt |
| | | cattttctgc | | | | |
| | 3361 | tcctcaagta | tcgagccagg | gagccgggtca | caaaggcaga | aatgctggag |
| 50 | | agtgtcctca | | | | |
| | 3421 | gaaattgcca | ggacttcttt | cccgtgatct | tcagcaaagc | ctccgagtac |
| | | ttgcagctgg | | | | |
| | 3481 | tctttggcat | cgagggtggg | gaagtgggtcc | ccatcagcca | cttgtagatc |
| | | cttgtcacct | | | | |
| 55 | 3541 | gcctgggcct | ctcctacgat | ggcctgctgg | gcgacaatca | ggtcatgccc |
| | | aagacaggcc | | | | |
| | 3601 | tcctgataat | cgtcctggcc | ataatcgcaa | tagaggggcg | ctgtgccctc |
| | | gaggagaaaa | | | | |

```

      3661 tctgggagga gctgagtatg ttggagggtgt ttgaggggag ggaggacagt
gtcttcgcac
      3721 atcccaggaa gctgctcatg caagatctgg tgcaggaaaa ctacctggag
taccggcagg
5      3781 tgcccggcag tgatcctgca tgctacgagt tcctgtgggg tccaagggcc
ctcattgaaa
      3841 ccagctatgt gaaagtcctg caccatacac taaagatcgg tggagaacct
cacatttcct
      3901 acccaccctt gcatgaacgg gctttgagag agggagaaga gtgagtctca
10 gcacatgttg
      3961 cagccagggc cagtgggagg ggggtctgggc cagtgcacct tccagggccc
catccattag
      4021 cttccactgc ctctgtgat atgaggccca ttcctgcctc tttgaagaga
gcagtcagca
15      4081 ttcttagcag tgagtttctg ttctgttgga tgactttgag atttatcttt
ctttcctgtt
      4141 ggaattgttc aaatgttcct tttaacaaat gggttgatga acttcagcat
ccaagtttat
      4201 gaatgacagt agtcacacat agtgctgttt atatagttta ggggtaagag
20 tcctgttttt
      4261 tattcagatt gggaaatcca ttccattttg tgagttgtca cataataaca
gcagtggaat
      4321 atgtatttgc ctatattgtg aacgaattag cagtaaaata catgatacaa
ggaactcaaa
25      4381 agatagttaa ttcttgcctt atacctcagt ctattatgta aaattaaaaa
tatgtgtatg
      4441 tttttgcttc tttgagaatg caaaagaaat taaatctgaa taaattcttc
ctgttcactg
      4501 gctcatttct ttaccattca ctcagcatct gctctgtgga aggccttggg
30 agtagtggg
  //

```

Human MAGE-3 antigen (MAGE-3) gene, complete cds.

```

35  ACCESSION   U03735
    VERSION    U03735.1  GI:468825
    SEQ ID NO  73

```

```

40  /translation="MPLEQRSQHCKPEEGLEARGEALGLVGAQAPATEEQEAASSSSTLVEVTLGE
VPAESPDPQPSPQGASSLPTTMNYPLWSQSYEDSSNQEEGPSTFPDLESEFQAALSRKVAELVH
FLLLKYRAREPVTKAEMLGSVVGNWQYFFPVI FSKASSSLQLVFGIELMEVDPIGHLIYIFATCLGL
SYDGLLGDNQIMPKAGLLIIVLAI IAREGDCAPEEKIWEELSVLEVFEGRSDILGDPKKLLTQHF
VQENYLEYRQVPGSDPACYEFLWGPRLVETS YVKVLHMHVKISGGPHISYPPLHEWVLREGEE"

```

```

45  SEQ ID NO  83
    ORIGIN

```

```

      1  acgcaggcag tgatgtcacc cagaccacac cccttcccc aatgccactt
cagggggtac
      61  tcagagtcag agacttggtc tgaggggagc agaagcaatc tgcagaggat
50  ggcggtccag
      121  gctcagccag gcatcaactt caggaccctg agggatgacc gaaggccccg
cccaccacc
      181  cccaactccc ccgacccccc caggatctac agcctcagga cccccgtccc
aatccttacc
55      241  ccttgcccca tcaccatctt catgcttacc tccaccccca tccgatcccc
atccaggcag
      301  aatccagttc caccctgcc cggaaccag ggtagtaccg ttgccaggat
gtgacgccac

```

| | | | | | | |
|----|------|-------------|-------------|------------|-------------|-------------|
| | 361 | tgacttgccg | attggagggtc | agaagaccgc | gagattctcg | ccctgagcaa |
| | | cgagcgacgg | | | | |
| | 421 | cctgacgtcg | gcggagggaa | gccggcccag | gctcgggtgag | gaggcaaggt |
| | | aagacgctga | | | | |
| 5 | 481 | gggaggactg | aggcgggcct | cacctcagac | agagggcctc | aaataatcca |
| | | gtgctgcctc | | | | |
| | 541 | tgctgccggg | cctggggccac | cccgcagggg | aagacttcca | ggctgggtcg |
| | | ccactacctc | | | | |
| 10 | 601 | accccgccga | ccccgcgcg | tttagccacg | gggaactctg | gggacagagc |
| | | ttaatgtggc | | | | |
| | 661 | cagggcaggg | ctggtttagaa | gaggtcaggg | cccacgctgt | ggcaggaatc |
| | | aaggtcagga | | | | |
| | 721 | ccccgagagg | gaactgaggg | cagcctaacc | accaccctca | ccaccattcc |
| | | cgtcccccaa | | | | |
| 15 | 781 | cacccaaccc | cacccccatc | ccccattccc | atccccaccc | ccacccttat |
| | | cctggcgagaa | | | | |
| | 841 | tccgggcttt | gcccctggta | tcaagtcacg | gaagctccgg | gaatggcggc |
| | | caggcacgtg | | | | |
| 20 | 901 | agtcctgagg | ttcacatcta | cggctaaggg | agggaaaggg | ttcgggtatcg |
| | | cgagtatggc | | | | |
| | 961 | cgttgggagg | cagcgaaagg | gcccaggcct | cctggaagac | agtggagtcc |
| | | tgaggggacc | | | | |
| | 1021 | cagcatgcca | ggacaggggg | cccactgtac | ccctgtctca | aaccgaggca |
| | | ccttttcatt | | | | |
| 25 | 1081 | cggctacggg | aatcctaggg | atgcagaccc | acttcagcag | gggggttgggg |
| | | cccagccctg | | | | |
| | 1141 | cgaggagtca | tggggaggaa | gaagagggag | gactgagggg | accttgaggat |
| | | ccagatcagt | | | | |
| 30 | 1201 | ggcaaccttg | ggctggggga | tgctgggcac | agtggccaaa | tgtgctctgt |
| | | gctcattgcg | | | | |
| | 1261 | ccttcagggt | gaccagagag | ttgagggctg | tgggtctgaag | agtgggactt |
| | | caggtcagca | | | | |
| | 1321 | gagggaggaa | tcccaggatc | tgcagggccc | aaggtgtacc | cccaaggggc |
| | | ccctatgtgg | | | | |
| 35 | 1381 | tggacagatg | cagtggtcct | aggatctgcc | aagcatccag | gtgaagagac |
| | | tgagggagga | | | | |
| | 1441 | ttgagggtag | ccctgggaca | gaatgcggac | tgggggcccc | ataaaaatct |
| | | gccctgctcc | | | | |
| 40 | 1501 | tgctgttacc | tcagagagcc | tgggcagggc | tgtcagctga | ggtccctcca |
| | | ttatcctagg | | | | |
| | 1561 | atcactgatg | tcaggggaagg | ggaagccttg | gtctgagggg | gctgcactca |
| | | gggcagtaga | | | | |
| | 1621 | gggaggctct | cagaccctac | taggagtggg | ggtgaggacc | aagcagtctc |
| | | ctcaccaggg | | | | |
| 45 | 1681 | gtacatggac | ttcaataaat | ttggacatct | ctcgttgtcc | tttccgggag |
| | | gacctgggaa | | | | |
| | 1741 | tgtatggcca | gatgtgggtc | ccctcatgtt | tttctgtacc | atatcaggta |
| | | tgtgagttct | | | | |
| 50 | 1801 | tgacatgaga | gattctcagg | ccagcagaag | ggagggatta | ggccctataa |
| | | ggagaaaggt | | | | |
| | 1861 | gagggccctg | agtgagcaca | gaggggatcc | tccaccccag | tagagtgggg |
| | | acctcacaga | | | | |
| | 1921 | gtctggccaa | ccctcctgac | agttctggga | atccgtgggt | gcgtttgctg |
| | | tctgcacatt | | | | |
| 55 | 1981 | gggggcccgt | ggattcctct | cccaggaatc | aggagctcca | ggaacaaggc |
| | | agtgaggact | | | | |
| | 2041 | tgggtctgagg | cagtgtcctc | aggtcacaga | gtagaggggg | ctcagatagt |
| | | gccaacggtg | | | | |

| | | | | | | |
|----|-------------|-------------|------------|-------------|------------|-------------|
| | 2101 | aaggtttgcc | ttggattcaa | accaagggcc | ccacctgccc | cagaacacat |
| | ggactccaga | | | | | |
| | 2161 | gcgcctggcc | tcacctcaa | tactttcagt | cctgcagcct | cagcatgcgc |
| 5 | tggccggatg | | | | | |
| | 2221 | tacctgagg | tgccctctca | cttcctcctt | caggttctga | ggggacaggc |
| | tgacctggag | | | | | |
| | 2281 | gaccagaggc | ccccggagga | gcactgaagg | agaagatctg | taagtaagcc |
| | tttggttagag | | | | | |
| 10 | 2341 | cctccaaggt | tccattcagt | actcagctga | ggtctctcac | atgctccctc |
| | tctccccagg | | | | | |
| | 2401 | ccagtgggtc | tccattgccc | agctcctgcc | cacactcccc | cctgttgccc |
| | tgaccagagt | | | | | |
| | 2461 | catcatgcct | cttgagcaga | ggagtcagca | ctgcaagcct | gaagaaggcc |
| | ttgaggcccc | | | | | |
| 15 | 2521 | aggagaggcc | ctgggcctgg | tgggtgcgca | ggctcctgct | actgaggagc |
| | aggaggctgc | | | | | |
| | 2581 | ctcctcctct | tctactctag | ttgaagtcac | cctgggggag | gtgcctgctg |
| | ccgagtcacc | | | | | |
| 20 | 2641 | agatcctccc | cagagtcctc | agggagcctc | cagcctcccc | actaccatga |
| | actaccctct | | | | | |
| | 2701 | ctggagccaa | tcctatgagg | actccagcaa | ccaagaagag | gaggggccaa |
| | gcaccttccc | | | | | |
| | 2761 | tgacctggag | tccgagttcc | aagcagcact | cagtaggaag | gtggccgagt |
| | tggttcattt | | | | | |
| 25 | 2821 | tctgctcctc | aagtatcgag | ccaggggagcc | ggtcacaaag | gcagaaatgc |
| | tggggagtgt | | | | | |
| | 2881 | cgtcggaaat | tggcagtatt | tctttcctgt | gatcttcagc | aaagcttcca |
| | gttccttgca | | | | | |
| 30 | 2941 | gctgggtcttt | ggcatcgagc | tgatggaagt | ggaccccatc | ggccacttgt |
| | acatctttgc | | | | | |
| | 3001 | cacctgcctg | ggcctctcct | acgatggcct | gctgggtgac | aatcagatca |
| | tgcccaaggc | | | | | |
| | 3061 | aggcctcctg | ataatcgtcc | tggccataat | cgcaagagag | ggcgactgtg |
| 35 | cccctgagga | | | | | |
| | 3121 | gaaaatctgg | gaggagctga | gtgtgttaga | ggtgtttgag | gggaggggaag |
| | acagtatctt | | | | | |
| | 3181 | gggggatccc | aagaagctgc | tcacccaaca | tttcgtgcag | gaaaactacc |
| | tggagtaccg | | | | | |
| 40 | 3241 | gcagggtcccc | ggcagtgatc | ctgcatgtta | tgaattcctg | tgggggtccaa |
| | gggccctcgt | | | | | |
| | 3301 | tgaaaccagc | tatgtgaaag | tcctgcacca | tatggtaaag | atcagtgagg |
| | gacctcacat | | | | | |
| | 3361 | ttcctaccca | cccctgcatg | agtgggtttt | gagagagggg | gaagagtgag |
| 45 | tctgagcacg | | | | | |
| | 3421 | agttgcagcc | agggccagtg | ggagggggtc | tgggccagtg | caccttcogg |
| | ggccgcatcc | | | | | |
| | 3481 | cttagtttcc | actgcctcct | gtgacgtgag | gcccattctt | cactctttga |
| | agcgagcagt | | | | | |
| 50 | 3541 | cagcattctt | agtagtgggt | ttctgttctg | ttggatgact | ttgagattat |
| | tctttgttcc | | | | | |
| | 3601 | ctgttgaggt | tgttcaaagt | ttccttttaa | cggatgggtg | aatgagcgtc |
| | agcatccagg | | | | | |
| | 3661 | tttatgaatg | acagtagtca | cacatagtcg | tgtttatata | gtttaggagt |
| | aagagtcttg | | | | | |
| 55 | 3721 | ttttttactc | aaattgggaa | atccattcca | ttttgtgaat | tgtgacataa |
| | taatagcagt | | | | | |
| | 3781 | ggtaaaagta | tttgcttaaa | attgtgagcg | aattagcaat | aacatacatg |
| | agataactca | | | | | |


```

      3841 agaaatcaaa agatagttga ttcttgccct gtacctcaat ctattctgta
aaattaaaca
      3901 aatatgcaaa ccaggatttc cttgacttct ttgagaatgc aagcgaaatt
aaatctgaat
5      3961 aaataattct tcctcttcac tggctcgttt cttttccggt cactcagcat
ctgctctgtg
      4021 ggaggccctg ggtagtagt ggggatgcta aggtaagcca gactcacgcc
taccatagg
      4081 gctgtagagc ctaggacctg cagtcataata attaagggtg tgagaagtcc
10 tgtaagatgt
      4141 agaggaaatg taagagagg gtgagggtgt ggcgctccgg gtgagagtag
tgagagtgtca
      4201 gtgc
//
15 Homo sapiens prostate stem cell antigen (PSCA) mRNA, complete
   cds.
   ACCESSION   AF043498
   VERSION     AF043498.1   GI:2909843
20 SEQ ID NO 79

   /translation="MKAVLLALLMAGLALQP GTALLCYSCKAQVS NEDCLQVENCTQLGEQCW
TARIRAVGLLTVISKGCSLNCVDDSDYYVGKKNITCCD TDLCNASGAHALQPAAILALLPA
LGLLLWGP GQL"
25 SEQ ID NO 87
   ORIGIN
      1 agggagaggc agtgaccatg aaggctgtgc tgcttgccct gttgatggca
ggcttgggccc
30      61 tgcagccagg cactgccctg ctgtgctact cctgcaaagc ccaggtgagc
aacgaggact
      121 gcctgcaggt ggagaactgc acccagctgg gggagcagtg ctggaccgcg
cgcacccgcg
      181 cagttggcct cctgaccgtc atcagcaaag gctgcagctt gaactgcgtg
35 gatgactcac
      241 aggactacta cgtgggcaag aagaacatca cgtgctgtga caccgacttg
tgcaacgcca
      301 gcggggccca tgccctgcag ccggctgccc ccacacctgc gctgctccct
gcaactcgccc
40      361 tgctgctctg gggacccggc cagctatagg ctctgggggg ccccgctgca
gccacactg
      421 ggtgtggtgc cccaggcctt tgtgccactc ctacacagaac ctggcccagt
gggagcctgt
      481 cctggttcct gaggcacatc ctaacgcaag tttgaccatg tatgtttgca
45 ccccttttcc
      541 ccnaaccctg accttcccat gggccttttc caggattccn accnngcaga
tcagtttttag
      601 tganacanat ccgcntgcag atggcccctc caaccntttt tgttgntggt
tccatggccc
50      661 agcatttttc acccttaacc ctgtgttcag gcacttnttc ccccaggaag
ccttccctgc
      721 ccacccattt tatgaattga gccaggtttg gtccgtggtg tccccgcac
ccagcagggg
      781 acaggcaatc aggaggggcc agtaaaggct gagatgaagt ggactgagta
55 gaactggagg
      841 acaagagttg acgtgagttc ctgggagttt ccagagatgg ggcctggagg
cctggaggaa

```

901 ggggccaggc ctcacatttg tggggntccc gaatggcagc ctgagcacag
 cgtaggccct
 961 taataaacac ctgttgata agccaaaaaa
 //

5

GLANDULAR KALLIKREIN 1 PRECURSOR (TISSUE KALLIKREIN)
 (KIDNEY/PANCREAS/SALIVARY GLAND KALLIKREIN).

10 ACCESSION P06870
 PID g125170
 VERSION P06870 GI:125170

SEQ ID NO 105
 ORIGIN

15 1 mwflvlclal slggtgaapp iqsrivggwe ceqhsqpwwa alyhfstfqc
 ggilvhrqvv
 61 ltaahcisdn yqlwlgrhnl fddentaqfv hvsesfphpg fnmsllenht
 rqadedyshd
 121 lmlrltpepa dtitdavkvv elptqepevg stclasgwgs iepenfsfpd
 20 dlqcvdlkil
 181 pndecakahv qkvtdfmlcv ghleggkdtc vgdsgggplmc dgvlqgvtsw
 gyvpcgtpnk
 241 psvavrvlsy vkwiedtia ns
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25

ELASTASE 2A PRECURSOR.

30 ACCESSION P08217
 PID g119255
 VERSION P08217 GI:119255

SEQ ID NO 106
 ORIGIN

35 1 mirtlllsltl vagalscgrp typyvtrvv ggeearpnsw pwqvslqyss
 ngkwyhtcgg
 61 slianswvlt aahciissrt yrvglgrhnl yvaesgslav svskivvhkd
 wnsnqiskgn
 121 diallklanp vsltldkiqla clppagtilp nnypcyvtgw grlqtngavp
 dvlqqgrllv
 40 181 vdyatcssa wwgssvktm icaggdgvls scngdsggpl ncqasdgrwq
 vhgivsfgr
 241 lgcnyyhkps vftrvsnyid winsviann
 //

45 pancreatic elastase IIB [Homo sapiens].
 ACCESSION NP_056933
 PID g7705648
 VERSION NP_056933.1 GI:7705648

50 SEQ ID NO 107
 ORIGIN

1 mirtlllsltl vagalscgvs tyapdmsrml ggeearpnsw pwqvslqyss
 ngqwyhtcgg
 61 slianswvlt aahciissri yrvmlgqhn1 yvaesgslav svskivvhkd
 55 wnsnqvskgn
 121 diallklanp vsltldkiqla clppagtilp nnypcyvtgw grlqtngalp
 ddlkqgrllv

181 vdyatcsss g wwgstvktnm icaggdgvic tcngdsggpl ncqasdgrwe
 vhgigsltsv
 241 lgcnyyykps iftrvsnynd winsviann
 //

5

PRAME Homo sapiens preferentially expressed antigen in melanoma
 (PRAME), mRNA.

10 ACCESSION NM_006115
 VERSION NM_006115.1 GI:5174640
 SEQ ID NO 77

/translation="MERRRLWGSIQSRYISMSVWTSPPRLVELAGQSLLKDEALAIAALELLPREL
 FPPLFMAAFDGRHSQTLKAMVQAWPFTCLPLGVLMKGQHLHLETFKAVLDGLDVLLAQEVRPRRWK
 15 LQVLDLRKNSHQDFWTVWSGNRASLYSFPEPEAAQPMTKRKVDGLSTEAEQPFIPVEVLVDLFLK
 EGACDELFSYLIEKVKRKKNVLRRLCCKKLKIFAMPMDIKMILKMVQLDSIEDLEVTCTWKLP
 KFSPLYLGQMINLRRLLLSHIHASSYISPEKEEQYIAQFTSQFLSIQCLQALYVDSLFFLRGRDQ
 LRHVMNPLETSLITNCRLSEGDMHLSQSPSVSLSVLSLGVMLTDVSPPEPLQALLERASATLQD
 20 LVFDECGITDDQLLALLPSLSHCSQLTTLSTFYGNSISISALQSLLOHLIGLSNLTHVLYPVP
 LESY EDIHGTLHLERLAYLHARLRELLCELGRPSMVWLSANPCPHCGDRTFYDPEPILCPCFMPN"

SEQ ID NO 85

ORIGIN

1 gcttcagggt acagctcccc cgcagccaga agccgggcct gcagcccctc
 25 agcaccgctc
 61 cgggacaccc caccgcttc ccaggcgtga cctgtcaaca gcaacttcgc
 ggtgtggtga
 121 actctctgag gaaaaacat tttgattatt actctcagac gtgcgtggca
 acaagtgact
 181 gagacctaga aatccaagcg ttggagggtcc tgaggccagc ctaagtcgct
 30 tcaaaatgga
 241 acgaaggcgt ttgtgggggt ccattcagag ccgatacatc agcatgagtg
 tgtggacaag
 301 cccacggaga cttgtggagc tggcagggca gagcctgctg aaggatgagg
 35 ccctggccat
 361 tgccgccctg gagttgctgc ccaggagct cttcccgcca ctcttcattg
 cagcctttga
 421 cgggagacac agccagaccc tgaaggcaat ggtgcaggcc tggcccttca
 cctgcctccc
 481 tctgggagtg ctgatgaagg gacaacatct tcacctggag accttcaaag
 40 ctgtgcttga
 541 tggacttgat gtgctccttg cccaggaggt tcgccccagg aggtggaaac
 ttcaagtgtc
 601 ggattttacgg aagaactctc atcaggactt ctggactgta tgggtctggaa
 45 acagggccag
 661 tctgtactca tttccagagc cagaagcagc tcagcccatg acaaagaagc
 gaaaagtaga
 721 tggtttgagc acagaggcag agcagccctt cattccagta gaggtgctcg
 tagacctgtt
 781 cctcaaggaa ggtgcctgtg atgaattgtt ctctacctc attgagaaag
 50 tgaagcgaaa
 841 gaaaaatgta ctacgcctgt gctgtaagaa gctgaagatt tttgcaatgc
 ccatgcagga
 901 tatcaagatg atcctgaaaa tgggtgcagct ggactctatt gaagatttgg
 55 aagtgacttg
 961 tacctggaag ctaccacact tggcgaaatt ttctccttac ctgggccaga
 tgattaatct

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1021 gcgtagactc ctcctctccc acatccatgc atcttcctac atttccccgg
agaaggaaga
1081 gcagtatatc gccagttca cctctcagtt cctcagtctg cagtgcctgc
aggctctcta
5 1141 tgtggactct ttatTTTTcc ttagaggccg cctggatcag ttgctcaggg
acgtgatgaa
1201 ccccttgga accctctcaa taactaactg ccggctttcg gaaggggatg
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1261 gtcccagagt cccagcgtca gtcagctaag tgtcctgagt ctaagtgggg
10 tcatgctgac
1321 cgatgtaagt cccgagcccc tocaagctct gctggagaga gcctctgcca
ccctccagga
1381 cctggctctt gatgagtgtg ggatcacgga tgatcagctc cttgccctcc
tgccctccct
1441 gagccactgc tcccagctta caaccttaag cttctacggg aattccatct
15 ccatatctgc
1501 cttgcagagt ctctgcagc acctcatcgg gctgagcaat ctgaccacg
tgctgtatcc
1561 tgtccccctg gagagttatg aggacatcca tggtaacctc cacctggaga
20 ggcttgcccta
1621 tctgcatgcc aggctcaggg agttgctgtg tgagttgggg cggcccagca
tggtctggct
1681 tagtgccaac ccctgtctc actgtgggga cagaacctc tatgaccgg
agcccatcct
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25 ttctgcatac
1801 ttggacacta aagccaggat gtgcatgcat cttgaagcaa caaagcagcc
acagtttcag
1861 acaaatgttc agtgtgagtg aggaaaacat gttcagttag gaaaaaacat
30 tcagacaaat
1921 gttcagttag gaaaaaaagg ggaagttggg gataggcaga tgttgacttg
aggagttaat
1981 gtgatctttg gggagataca tcttatagag ttagaaatag aatctgaatt
tctaaaggga
2041 gattctggct tgggaagtac atgtaggagt taatccctgt gtagactgtt
35 gtaaagaaac
2101 tgttgaaaat aaagagaagc aatgtgaagc aaaaaaaaaa aaaaaaaa

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40 //

CEA Homo sapiens carcinoembryonic antigen-related cell adhesion molecule 5 (CEACAM5), mRNA.

ACCESSION NM_004363

45 VERSION NM_004363.1 GI:11386170

SEQ ID NO 88

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50 PNASLLIQNIIQNDTGFYTLHVIKSDLVNEEATGQFRVYPELPKPSISSNNSKPVEDK
DAVAFTCEPETQDATYLLWVNNQSLPVS PRLQLSNGNRTLTLFNVTRNDTASYKCETQ

```

NPVSARRSDSVILNVLYGPDAPTISPLNTSYRSGENLNLSCHAASNPPAQYSWFVNGT
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 VEDEDAVALTCEPEIQNTTYLWWVNNQSLPVSRLQLSNDNRTLTLSSVTRNDVGPYE
 CGIQNELSDHSDPVLNVLYGPDPTISPSYTYRPGVNLSSLCHAASNPPAQYSWL
 5 IDGNIQQHTQELFISNITEKNSGLYTCQANNSASGHSRTTVKTTITVSAELPKPSISSN
 NSKPVEDKDAVAFTCEPEAQNTTYLWWVNGQSLPVSRLQLSNGNRRTLTLFNVTRNDA
 RAYVCGIQNSVSANRSDPVTLDVLYGPDTPIIISPPDSSYLSGANLNLSCHSASNPSPQ
 YSWRINGIPQQHTQVLFIAKITPNNNGTYACFVSNLATGRNNSIVKSITVSASGTSPG
 LSAGATVGIMIGVLVGVALI"

10

SEQ ID NO 89

ORIGIN

1 ctcagggcag agggaggaag gacagcagac cagacagtca cagcagcctt
 gacaaaacgt
 15 61 tcctggaact caagctcttc tccacagagg aggacagagc agacagcaga
 gaccatggag
 121 tctccctcgg cccctcccca cagatggtgc atcccctggc agaggctcct
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 20 atccacgccg
 241 ttcaatgtcg cagaggggaa ggaggtgctt ctacttgtcc acaatctgcc
 ccagcatctt
 301 tttggctaca gctggtacaa aggtgaaaga gtggatggca accgtcaa
 tataggatat
 25 361 gtaataggaa ctcaacaagc taccacaggg ccgcataca gtggtcgaga
 gataatatac
 421 cccaatgcat cctgctgat ccagaacatc atccagaatg acacaggatt
 ctacacccta
 481 cacgtcataa agtcagatct tgtgaatgaa gaagcaactg gccagttccg
 30 ggtatacccg
 541 gagctgcca agccctccat ctccagcaac aactccaaac ccgtggagga
 caaggatgct
 601 gtggccttca cctgtgaacc tgagactcag gacgcaacct acctgtggtg
 ggtaaacaat
 35 661 cagagcctcc cggtcagtcc caggctgcag ctgtccaatg gcaacaggac
 cctcactcta
 721 ttcaatgtca caagaaatga cacagcaagc taaaatgtg aaaccagaa
 cccagtgagt

| | | | | | | |
|----|------|-------------|-------------|------------|------------|------------|
| | 781 | gccaggcgca | gtgattcagt | catcctgaat | gtcctctatg | gcccggatgc |
| | | ccccaccatt | | | | |
| | 841 | tcccctctaa | acacatctta | cagatcaggg | gaaaatctga | acctctcctg |
| | | ccacgcagcc | | | | |
| 5 | 901 | tctaaccac | ctgcacagta | ctcttggttt | gtcaatggga | ctttccagca |
| | | atccacccaa | | | | |
| | 961 | gagctcttta | tcccacaacat | cactgtgaat | aatagtggat | cctatacgtg |
| | | ccaagcccat | | | | |
| | 1021 | aactcagaca | ctggcctcaa | taggaccaca | gtcacgacga | tcacagtcta |
| 10 | | tgcagagcca | | | | |
| | 1081 | cccaaaccct | tcatcaccag | caacaactcc | aaccccgtgg | aggatgagga |
| | | tgctgtagcc | | | | |
| | 1141 | ttaacctgtg | aacctgagat | tcagaacaca | acctacctgt | ggtgggtaaa |
| | | taatcagagc | | | | |
| 15 | 1201 | ctcccgggtca | gtcccaggct | gcagctgtcc | aatgacaaca | ggaccctcac |
| | | tctactcagt | | | | |
| | 1261 | gtcacaagga | atgatgtagg | accctatgag | tgtggaatcc | agaacgaatt |
| | | aagtgttgac | | | | |
| | 1321 | cacagcgacc | cagtcatcct | gaatgtcctc | tatggcccag | acgaccccac |
| 20 | | catttcccc | | | | |
| | 1381 | tcatacacct | attaccgtcc | aggggtgaac | ctcagcctct | cctgccatgc |
| | | agcctctaac | | | | |
| | 1441 | ccacctgcac | agtattcttg | gctgattgat | gggaacatcc | agcaacacac |
| | | acaagagctc | | | | |
| 25 | 1501 | tttatctcca | acatcactga | gaagaacagc | ggactctata | cctgccaggc |
| | | caataactca | | | | |
| | 1561 | gccagtggcc | acagcaggac | tacagtcaag | acaatcacag | tctctgcgga |
| | | gctgcccagg | | | | |
| | 1621 | ccctccatct | ccagcaacaa | ctccaaaccc | gtggaggaca | aggatgctgt |
| 30 | | ggccttcacc | | | | |
| | 1681 | tgtgaacctg | aggctcagaa | cacaacctac | ctgtggtggg | taaatggtca |
| | | gagcctccca | | | | |
| | 1741 | gtcagtccca | ggctgcagct | gtccaatggc | aacaggaccc | tactctatt |
| | | caatgtcaca | | | | |
| 35 | 1801 | agaaatgacg | caagagccta | tgtatgtgga | atccagaact | cagtgagtgc |
| | | aaaccgcagt | | | | |
| | 1861 | gacccagtca | ccctggatgt | cctctatggg | cgggacaccc | ccatcatttc |
| | | ccccccagac | | | | |

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      1921  tcgtcttacc  ttctcgggagc  gaacctcaac  ctctcctgcc  actcggcctc
taacccatcc
      1981  ccgcagtatt  cttggcgtat  caatgggata  ccgcagcaac  acacacaagt
tctctttatc
5      2041  gccaaaatca  cgccaaataa  taacgggacc  tatgcctggt  ttgtctctaa
cttggctact
      2101  ggccgcaata  attccatagt  caagagcatc  acagtctctg  catctggaac
ttctcctggg
      2161  ctctcagctg  gggccactgt  cggcatcatg  attggagtgc  tggttggggg
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      2221  tagcagccct  ggtgtagttt  cttcatttca  ggaagactga  cagttgtttt
gcttcttcct
      2281  taaagcattt  gcaacagcta  cagtctaaaa  ttgcttcttt  accaaggata
tttacagaaa
15      2341  agactctgac  cagagatcga  gaccatccta  gccaacatcg  tgaaacccca
tctctactaa
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ctcgggaggg
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20  agatcgcacc
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aaaagaagac
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gaatttccaa
25      2641  aactttaatg  aactaactga  cagcttcatg  aaactgtcca  ccaagatcaa
gcagagaaaa
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aatgtcttgt
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30  caatttgata
      2821  aaatataact  ttgtgaacaa  aaattgagac  atttacattt  tctccctatg
tggtcgcctc
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ttgcacaagt
35      2941  tcaataaaaa  tctgctcttt  gtataacaga  aaaa
//

```

Her2/Neu Human tyrosine kinase-type receptor (HER2) mRNA, complete cds.

ACCESSION M11730
 VERSION M11730.1 GI:183986
 SEQ ID NO 90

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 10 DTFESMPNPEGRYTFGASCVTACPYNYLSTDVGSCTLVCPLHNQEVTAEDGTQRCEKC
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SEQ ID NO 91

ORIGIN Chromosome 17q21-q22.

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| | 781 | gattgtcaga | gcctgacgcg | cactgtctgt | gccggtggct | gtgcccgctg |
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| | 841 | ctgcccactg | actgctgcca | tgagcagtg | gctgccggct | gcacggggccc |
| 20 | | caagcactct | | | | |
| | 901 | gactgcctgg | cctgcctcca | cttcaaccac | agtggcatct | gtgagctgca |
| | | ctgcccagcc | | | | |
| | 961 | ctggtcacct | acaacacaga | cacgtttgag | tccatgcccc | atcccagagg |
| | | ccggtataca | | | | |
| 25 | 1021 | ttcggcgcca | gctgtgtgac | tgccctgtccc | tacaactacc | tttctacgga |
| | | cgtgggatcc | | | | |
| | 1081 | tgcacctctg | tctgccccct | gcacaaccaa | gaggtgacag | cagaggatgg |
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| | 1141 | tgtgagaagt | gcagcaagcc | ctgtgcccga | gtgtgctatg | gtctgggcat |
| 30 | | ggagcacttg | | | | |
| | 1201 | cgagagggtga | gggcagttac | cagtgccaat | atccaggagt | ttgctggctg |
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| | 1261 | tttgggagcc | tggcatttct | gccggagagc | tttgatgggg | accagcctc |
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| 35 | 1321 | ccgctccagc | cagagcagct | ccaagtgttt | gagactctgg | aagagatcac |
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| | | cctgcaagta | | | | |

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|----|------|------------|------------|-------------|-------------|-------------|
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| | 1501 | agctggctgg | ggctgcgctc | actgaggga | ctgggcagtg | gactggccct |
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| | 1621 | caagctctgc | tccacactgc | caaccggcca | gaggacgagt | gtgtgggcga |
| | | gggcctggcc | | | | |
| | 1681 | tgccaccagc | tgtgcgcccg | agggcactgc | tgggggtccag | ggcccaccca |
| 10 | | gtgtgtcaac | | | | |
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| | | agccagccct | | | | |
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| | 2401 | gccatcaaag | tggtgagggg | aaacacatcc | cccaaagcca | acaagaaat |
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|----|------|-------------|-------------|-------------|------------|------------|
| | 2581 | cgggaaaacc | gcggaacgcct | gggctcccag | gacctgctga | actggtgtat |
| | | gcagattgcc | | | | |
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| 5 | 2701 | gtgctggtca | agagtcccaa | ccatgtcaaa | attacagact | tcgggctggc |
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| 25 | 3301 | tctaccagga | gtggcggtgg | ggacctgaca | ctagggctgg | agccctctga |
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| 30 | | ccctctacag | | | | |
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| | | ccagccccct | | | | |
| 35 | 3601 | tcgccccgag | agggccctct | gcctgctgcc | cgacctgctg | gtgccactct |
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30

H.sapiens mRNA for SCP1 protein.

ACCESSION X95654

VERSION X95654.1 GI:1212982

SEQ ID NO 92

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 5 KQFEKIAEELKGTEQELIGLLQAREKEVHDLEIQLTAITTSEQYYSKEVKDLKTELEN
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 10 EQSSLRASLEIELSNLKAELLSVKKQLEIEREEKEKLKREAKENTATLKEKKDKKTQT
 FLLETPEIYWKLDSKAVPSQTVSRNFTSVDHGISKDKRDYLWTSKNTLSTPLPKAYT
 VKTPTKPKLQQRENLPPIEESKKRKMAREFDINSDSSETTDLMSVSEEETLKTLY
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 KLFV"

15

SEQ ID NO 93

ORIGIN

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| | | aaaccaggca | | | | |
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| | | gggaacttcg | | | | |
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| | | attatgaaaa | | | | |
| | 841 | aatccaacac | cttgaacaag | aatacaagaa | ggaaataaat | gacaaggaaa |
| | | agcaggatc | | | | |
| | 901 | actactattg | atccaaatca | ctgagaaaga | aaataaaatg | aaagatttaa |
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| | 961 | agaggaatcc | agagataaag | ttaatcaatt | agaggaaaag | acaaaattac |
| | | agagtgtgaaa | | | | |
| | 1021 | cttaaaacaa | tcaattgaga | aacagcatca | tttgactaaa | gaactagaag |
| | | atattaaagt | | | | |
| 15 | 1081 | gtcattacaa | agaagtgtga | gtactcaaaa | ggcttttagag | gaagatttac |
| | | agatagcaac | | | | |
| | 1141 | aaaaacaatt | tgtcagctaa | ctgaagaaaa | agaaactcaa | atggaagaat |
| | | ctaataaagc | | | | |
| | 1201 | tagagctgct | cattcgtttg | tggttactga | atgtgaaact | actgtctgca |
| 20 | | gcttggaaga | | | | |
| | 1261 | attattgaga | acagaacagc | aaagattgga | aaaaaatgaa | gatcaattga |
| | | aaatacttac | | | | |
| | 1321 | catggagctt | caaaagaaat | caagtgaagc | ggaagagatg | actaagctta |
| | | caaataacaa | | | | |
| 25 | 1381 | agaagtagaa | cttgaagaat | tgaaaaaagt | cttgggagaa | aaggaaacac |
| | | ttttatatga | | | | |
| | 1441 | aaataaacia | tttgagaaga | ttgctgaaga | attaaaagga | acagaacaag |
| | | aactaattgg | | | | |
| | 1501 | tcttctccaa | gccagagaga | aagaagtaca | tgatttgga | atacagttaa |
| 30 | | ctgccattac | | | | |
| | 1561 | cacaagtga | cagtattatt | caaaagaggt | taaagatcta | aaaactgagc |
| | | ttgaaaacga | | | | |
| | 1621 | gaagcttaag | aataactgaat | taacttcaca | ctgcaacaag | ctttcactag |
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| | 1741 | taataacaaa | aagcaagaag | aaaggatggt | gaaacaaata | gaaaatcttc |
| | | aagaaacaga | | | | |

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|----|------|------------|------------|------------|------------|-------------|
| | 1801 | aacccaatta | agaaatgaac | tagaatatgt | gagagaagag | ctaaaacaga |
| | | aaagagatga | | | | |
| | 1861 | agttaaatgt | aaattggaca | agagtgaaga | aaattgtaac | aattttaagga |
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| 5 | 1921 | aaataaaaac | aagtatatgt | aagaacttca | gcaggagaat | aaggccttga |
| | | aaaaaaaagg | | | | |
| | 1981 | tacagcagaa | agcaagcaac | tgaatgttta | tgagataaag | gtcaataaat |
| | | tagagttaga | | | | |
| | 2041 | actagaaagt | gccaaacaga | aatttggaga | aatcacagac | acctatcaga |
| 10 | | aagaaattga | | | | |
| | 2101 | ggacaaaaag | atatcagaag | aaaatctttt | ggaagagggt | gagaaagcaa |
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| | | aaatagctga | | | | |
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| | | gagcatcttt | | | | |
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| 20 | | aacttgaaat | | | | |
| | 2401 | agaaagagaa | gagaaggaaa | aactcaaaag | agaggcaaaa | gaaaacacag |
| | | ctactcttaa | | | | |
| | 2461 | agaaaaaaaa | gacaagaaaa | cacaaacatt | tttattggaa | acacctgaaa |
| | | tttattggaa | | | | |
| 25 | 2521 | attggattct | aaagcagttc | cttcacaaac | tgtatctcga | aatttcacat |
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| | 2581 | tggcatatcc | aaagataaaa | gagactatct | gtggacatct | gccaaaaata |
| | | ctttatctac | | | | |
| | 2641 | accattgcca | aaggcatata | cagtgaagac | accaacaaaa | ccaaaactac |
| 30 | | agcaaagaga | | | | |
| | 2701 | aaacttgaat | ataccattg | aagaaagtaa | aaaaaagaga | aaaatggcct |
| | | ttgaatttga | | | | |
| | 2761 | tattaattca | gatagttcag | aaactactga | tcttttgagc | atggtttcag |
| | | aagaagagac | | | | |
| 35 | 2821 | attgaaaaca | ctgtatagga | acaataatcc | accagcttct | catctttgtg |
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2941 aaaaatgcgg gaggaccgtt gggctgtaat tgctaaaatg gatagaaaaa
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Homo sapiens synovial sarcoma, X breakpoint 4 (SSX4), mRNA.

20 ACCESSION NM_005636
VERSION NM_005636.1 GI:5032122
SEQ ID NO 94

/translation="MNGDDAFARRPRDDAQISEKLRKAFDDIAKYFSKKEWEKMKSSSEKIVY
25 VYMKLNIEVMTKLGFKVTLPPFMRSKRAADFHGNDGNDNRNHRNQVERPQMTFG
SLQRIFFPKIMPKKPAEEENGLKEVPEASGPQNDGKQLCPPGNPSTLEKINKTSGPKRG
KHAWTHRLRERKQLVVYEEISDPEEDDE"

SEQ ID NO 95

30 ORIGIN

1 atgaacggag acgacgcctt tgcaaggaga cccagggatg atgctcaa
atcagagaag
61 ttacgaaagg ccttcgatga tattgcaaaa tacttctcta agaaagagt
ggaaaagatg
35 121 aaatcctcgg agaaaatcgt ctatgtgtat atgaagctaa actatgaggt
catgactaaa
181 ctaggtttca aggtcaccct cccacctttc atgcgtagta aacgggctgc
agacttccac

241 gggaaatgatt ttggtaacga tcgaaaccac aggaatcagg ttgaacgtcc
 tcagatgact
 301 ttccggcagcc tccagagaat cttcccgaag atcatgcccagaagccagc
 agaggaagaa
 5 361 aatggtttga aggaagtgcc agaggcatct ggcccacaaa atgatgggaa
 acagctgtgc
 421 cccccgggaa atccaagtac cttggagaag attaacaaga catctggacc
 caaaagggg
 481 aaacatgcct ggaccacag actgcgtgag agaaagcagc tggtggttta
 10 tgaagagatc
 541 agcgaccctg aggaagatga cgagtaactc ccctcg

U19142. Human GAGE-1 prot...[gi:914898]

15 LOCUS HSU19142 646 bp mRNA linear
 DEFINITION Human GAGE-1 protein mRNA, complete cds.
 ACCESSION U19142
 VERSION U19142.1 GI:914898

20 SEQ ID No. 96
 /translation="MSWRGRSTYRPRPRRYVEPPEMIGPMRPEQFSDEVEPATPEEGE
 PATQRQDPAAAQEGEDEGASAGQGPKPEADSQEQGHPQTGCECEDGPDGQEMDPNPE
 EVKTPEEEMRSHYVAQTGILWLLMNNCFLNLSPRKP"

25
 SEQ ID NO. 97
 1 ctgccgtccg gactcttttt cctctactga gattcatctg tgtgaaatat
 gagttggcga
 61 ggaagatcga cctatcggcc tagaccaaga cgctacgtag agcctcctga
 30 aatgattggg
 121 cctatcggcc ccgagcagtt cagtgatgaa gtggaaccag caacacctga
 agaaggggaa
 181 ccagcaactc aacgtcagga tcctgcagct gctcaggagg gagaggatga
 gggagcatct
 35 241 gcaggtcaag ggccgaagcc tgaagctgat agccaggaaac agggtcaccc
 acagactggg
 301 tgtgagtgtg aagatgggcc tgatgggcag gagatggacc cgccaaatcc
 agaggaggtg

361 aaaacgcctg aagaagagat gaggtctcac tatgttgccc agactgggat
 tctctggctt
 421 ttaatgaaca attgcttctt aaatctttcc ccacggaaac cttgagtga
 tgaaatatca
 5 481 aatggcgaga gaccgttttag ttcctatcat ctgtggcatg tgaagggcaa
 tcacagtgtt
 541 aaaagaagac atgctgaaat gttgcaggct gctcctatgt tggaaaattc
 ttcattgaag
 601 ttctcccaat aaagctttac agccttctgc aaagaaaaaa aaaaaa
 10 //

NM_001168. Homo sapiens bacu...[gi:4502144]
 LOCUS BIRC5 1619 bp mRNA linear
 DEFINITION Homo sapiens baculoviral IAP repeat-containing 5
 15 (survivin) (BIRC5), mRNA.
 ACCESSION NM_001168
 VERSION NM_001168.1 GI:4502144

SEQ ID NO. 98
 20 /translation="MGAPTLPPAWQPFLKDHRI STFKNWPFLEGC ACTPERMAEAGFI
 HCPTENEPDLAQCF FCFKELEGWEPDDDDPIEEHKKHSSGCAFLSVKKQFEELTLGEFL
 KLDRE RAKNKIAKETNNKKKEFEETAKKVRRAIEQLAAMD"

25 SEQ ID NO. 99
 1 ccgccagatt tgaatcgcg gacccgttgg cagaggtggc ggcggcggca
 tgggtgcccc
 61 gacgttgccc cctgcctggc agccctttct caaggaccac cgcattctta
 cattcaagaa
 30 121 ctggcccttc ttggagggtc gcgcctgcac cccggagcgg atggccgagg
 ctggcttcat
 181 ccaactgcccc actgagaacg agccagactt ggcccagtgt ttctttctgct
 tcaaggagct
 241 ggaaggctgg gagccagatg acgaccccat agaggaacat aaaaagcatt
 35 cgtccggttg
 301 cgctttcctt tctgtcaaga agcagtttga agaattaacc cttggtgaat
 ttttgaaact
 361 ggacagagaa agagccaaga acaaaattgc aaaggaaacc aacaataaga
 agaaagaatt

| | | | | | | |
|----|------|------------|------------|------------|------------|------------|
| | 421 | tgaggaaact | gcgaagaaag | tgcgccgtgc | catcgagcag | ctggctgcca |
| | | tggattgagg | | | | |
| | 481 | cctctggccg | gagctgcctg | gtcccagagt | ggctgcacca | cttccagggg |
| | | ttattccctg | | | | |
| 5 | 541 | gtgccaccag | ccttcctgtg | ggccccttag | caatgtctta | ggaaaggaga |
| | | tcaacatttt | | | | |
| | 601 | caaattagat | gtttcaactg | tgtcctgtt | ttgtcttgaa | agtggcacca |
| | | gaggtgcttc | | | | |
| | 661 | tgcctgtgca | gcgggtgctg | ctggtaacag | tggctgcttc | tctctctctc |
| 10 | | tctctttttt | | | | |
| | 721 | gggggctcat | ttttgctgtt | ttgattcccg | ggcttaccag | gtgagaagtg |
| | | agggaggaag | | | | |
| | 781 | aaggcagtgt | cccttttgct | agagctgaca | gctttgttcg | cgtgggcaga |
| | | gccttccaca | | | | |
| 15 | 841 | gtgaatgtgt | ctggacctca | tgttggtgag | gctgtcacag | tcctgagtgt |
| | | ggacttggca | | | | |
| | 901 | ggtgcctgtt | gaatctgagc | tgcaggttcc | ttatctgtca | cacctgtgcc |
| | | tcctcagagg | | | | |
| | 961 | acagtttttt | tgttggtgtg | tttttttggt | tttttttttt | ggtagatgca |
| 20 | | tgacttgtgt | | | | |
| | 1021 | gtgatgagag | aatggagaca | gagtccttgg | ctcctctact | gtttaacaac |
| | | atggctttct | | | | |
| | 1081 | tattttgttt | gaattgttaa | ttcacagaat | agcacaaact | acaattaaaa |
| | | ctaagcacia | | | | |
| 25 | 1141 | agccattcta | agtcattggg | gaaacggggg | gaacttcagg | tggatgagga |
| | | gacagaatag | | | | |
| | 1201 | agtgatagga | agcgtctggc | agatactcct | tttgccactg | ctgtgtgatt |
| | | agacaggccc | | | | |
| | 1261 | agtgagccgc | ggggcacatg | ctggccgctc | ctccctcaga | aaaaggcagt |
| 30 | | ggcctaaatc | | | | |
| | 1321 | ctttttaaat | gacttggctc | gatgctgtgg | gggactgggt | gggctgctgc |
| | | aggccgtgtg | | | | |
| | 1381 | tctgtcagcc | caaccttcac | atctgtcacg | ttctccacac | gggggagaga |
| | | cgcagtccgc | | | | |
| 35 | 1441 | ccagggtccc | gctttctttg | gaggcagcag | ctcccgagg | gctgaagtct |
| | | ggcgtaagat | | | | |
| | 1501 | gatggatttg | attcgccctc | ctccctgtca | tagagctgca | gggtggattg |
| | | ttacagcttc | | | | |

1561 gctggaaacc tctggaggtc atctcggctg ttcctgagaa ataaaaagcc
 tgtcatttc
 //

5

U06452. Human melanoma an...[gi:476131]

LOCUS HSU06452 1524 bp mRNA linear

DEFINITION Human melanoma antigen recognized by T-cells (MART-1)
 mRNA.

10 ACCESSION U06452

VERSION U06452.1 GI:476131

SEQ ID NO.100

/translation="MPREDAHFYGYPKKGHGHSTTAEEAAGIGILTVILGVLLIG

15

CWYCRRRNGYRALMDKSLHVGTCALTRRCPEGFDRDSKVSLEKNCEPVVPNAPP
 AYEKLSAEQSPPPYSP"

SEQ ID NO. 101

20 1 agcagacaga ggactctcat taaggaaggt gtccctgtgcc ctgaccctac
 aagatgccaa
 61 gagaagatgc tcacttcac tcacttcac tatgggtacc ccaagaaggg gcacggccac
 tcttacacca
 121 cggctgaaga ggccgctggg atcggcatcc tgacagtgat cctgggagtc
 25 ttactgctca
 181 tcggctggtg gtattgtaga agacgaaatg gatacagagc cttgatggat
 aaaagtcttc
 241 atgttggcac tcaatgtgcc ttaacaagaa gatgccacac agaagggttt
 gatcatcggg
 30 301 acagcaaagt gtctcttcaa gagaaaaact gtgaacctgt ggttcccaat
 gctccacctg
 361 cttatgagaa actctctgca gaacagtcac caccacctta ttcaccttaa
 gagccagcga
 421 gacacctgag acatgctgaa attatttctc tcacactttt gcttgaattt
 35 aatacagaca
 481 tctaattgtc tccttttgaa tgggtgtagga aaaatgcaag ccatctctaa
 taataagtca
 541 gtgttaaaat tttagtaggt ccgctagcag tactaatcat gtgaggaaat
 gatgagaaat

```

        601 attaaattgg gaaaactcca tcaataaatg ttgcaatgca tgatactatc
        tgtgccagag
        661 gtaatgttag taaatccatg gtgttatatt ctgagagaca gaattcaagt
        gggatattctg
5        721 gggccatcca atttctcttt acttgaaatt tggctaataa caaactagtc
        aggttttcga
        781 accttgaccg acatgaactg tacacagaat tgttccagta ctatggagtg
        ctcacaaagg
        841 atacttttac aggttaagac aaagggttga ctggcctatt tatctgatca
10      agaàcatgtc
        901 agcaatgtct ctttgtgctc taaaattcta ttatactaca ataatatatt
        gtaaagatcc
        961 tatagctctt tttttttgag atggagtttc gcttttgttg cccaggctgg
        agtgcaatgg
15      1021 cgcgatcttg gctcaccata acctccgcct cccaggttca agcaattctc
        ctgccttagc
        1081 ctcttgagta gctgggatta caggcgtgcg ccactatgcc tgactaattt
        tgtagtttta
        1141 gtagagacgg ggtttctcca tgttggtcag gctgggtctca aactcctgac
20      ctgaggtgat
        1201 ctgcccgcct cagcctccca aagtgctgga attacaggcg tgagccacca
        cgcttggtg
        1261 gatcctatat cttaggtaag acatataacg cagtctaatt acatttcact
        tcaaggctca
25      1321 atgctattct aactaatgac aagtattttc tactaaacca gaaattggta
        gaaggattta
        1381 aataagtaaa agctactatg tactgcctta gtgctgatgc ctgtgtactg
        ccttaaattgt
        1441 acctatggca atttagctct cttgggttcc caaatccctc tcacaagaat
30      gtgcagaaga
        1501 aatcataaag gatcagagat tctg
        //

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U19180. Human B melanoma ...[gi:726039]

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35  LOCUS      HSU19180              1004 bp    mRNA    linear
     DEFINITION Human B melanoma antigen (BAGE) mRNA, complete cds.
     ACCESSION  U19180
     VERSION    U19180.1  GI:726039

```

SEQ IS NO. 102

/translation="MAARAVFLALSAQLLQARLMKEESPVVSWRLEPEDGTALCFIF"

SEQ ID NO. 103

```
5           1  cgccaattta  gggctctccgg  tatctcccgc  tgagctgctc  tgttcccggc
            ttagaggacc
            61  aggagaaggg  ggagctggag  gctggagcct  gtaacaccgt  ggctcgtctc
            actctggatg
            121  gtggtggcaa  cagagatggc  agcgcagctg  gagtgttagg  agggcggcct
10  gagcggtagg
            181  agtggggctg  gagcagtaag  atggcggcca  gagcggtttt  tctggcattg
            tctgcccagc
            241  tgctccaagc  caggctgatg  aaggaggagt  cccctgtggg  gagctggagg
            ttggagcctg
15           301  aagacggcac  agctctgtgc  ttcatcttct  gaggttgtgg  cagccacggg
            gatggagacg
            361  gcagctcaac  aggagcaata  ggaggagatg  gagtttctact  gtgtcagcca
            ggatgggtctc
            421  gatctcctga  cctcgtgatc  cgcccgctt  ggccttccaa  agtgccgaga
20  ttacagcgat
            481  gtgcattttg  taagcacttt  ggagccacta  tcaaagtctg  tgaagagaaa
            tgtaccagaa
            541  tgtatcatta  tccttgtgct  gcaggagccg  gctcctttca  ggatttcagt
            cacatcttcc
25           601  tgctttgtcc  agaacacatt  gaccaagctc  ctgaaagatg  taagtttact
            acgcatagac
            661  ttttaaactt  caaccaatgt  atttactgaa  aataacaaat  gttgtaaatt
            ccctgagtgt
            721  tattctactt  gtattaaaag  gtaataatac  ataatcatta  aaatctgagg
30  gatcattgcc
            781  agagattggt  ggggagggaa  atgttatcaa  cggtttcatt  gaaattaaat
            ccqaaaagtt
            841  atttcctcag  aaaaatcaaa  taaagtttgc  atgtttttta  ttcttaaaac
            attttaaaaa
35           901  cactgtaga  atgatgtaaa  tagggactgt  gcagtatttc  tgacatatac
            tataaaatta
            961  ttaaaaagtc  aatcagtatt  caacatcttt  tacactaaaa  agcc
//
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The teachings and embodiments disclosed in any of the publications, including patents, patent publications and non-patent publications, disclosed herein are contemplated as supporting principals and embodiments related to and useful in connection with the present invention.

5 The invention illustratively described herein suitably may be practiced in the absence of any element or elements, limitation or limitations which is not specifically disclosed herein. The terms and expressions which have been employed are used as terms of description and not of limitation, and there is no intention that in the use of such terms and expressions indicates the exclusion of equivalents of the features shown and described or portions thereof. It is recognized that various modifications are possible within the scope of the invention claimed. Thus, it should
10 be understood that although the present invention has been specifically disclosed by preferred embodiments and optional features, modification and variation of the concepts herein disclosed may be resorted to by those skilled in the art, and that such modifications and variations are considered to be within the scope of the embodiments of this invention.

15

WHAT IS CLAIMED IS:

1. A polypeptide, comprising a component selected from the group consisting of:
 - (i) a polypeptide epitope having the sequence as disclosed in TABLE 1B;
 - (ii) an epitope cluster comprising the polypeptide of (i);
 - (iii) a polypeptide having substantial similarity to (i) or (ii);
 - (iv) a polypeptide having functional similarity to any of (i) through (iii); and
 - (v) a nucleic acid encoding the polypeptide of any of (i) through (iv).
2. The polypeptide of claim 1, wherein the polypeptide is immunologically active.
3. The polypeptide of claim 1, wherein the polypeptide is less than about 30 amino acids in length.
4. The polypeptide of claim 1, wherein the polypeptide is 8 to 10 amino acids in length.
5. The polypeptide of claim 1, wherein the substantial or functional similarity comprises addition of at least one amino acid.
6. The polypeptide of claim 5, wherein the at least one additional amino acid is at an N-terminus of the polypeptide.
7. The polypeptide of claim 1, wherein the substantial or functional similarity comprises a substitution of at least one amino acid.
8. The polypeptide of claim 1, the polypeptide having affinity to an HLA-A2 molecule.
9. The polypeptide of claim 8, wherein the affinity is determined by an assay of binding.
10. The polypeptide of claim 8, wherein the affinity is determined by an assay of restriction of epitope recognition.
11. The polypeptide of claim 8, wherein the affinity is determined by a prediction algorithm.
12. The polypeptide of claim 1, the polypeptide having affinity to an HLA-B7 or HLA-B51 molecule.
13. The polypeptide of claim 1, wherein the polypeptide is a housekeeping epitope.
14. The polypeptide of claim 1, wherein the polypeptide corresponds to an epitope displayed on a tumor cell.
15. The polypeptide of claim 1, wherein the polypeptide corresponds to an epitope displayed on a neovasculature cell.
16. The polypeptide of claim 1, wherein the polypeptide is an immune epitope.
17. The polypeptide of claim 1, wherein the polypeptide is encoded by a nucleic acid.

18. A composition comprising the polypeptide of claim 1 and a pharmaceutically acceptable adjuvant, carrier, diluent, or excipient.
19. The composition of claim 18, where the adjuvant is a polynucleotide.
20. The composition of claim 19 wherein the polynucleotide comprises a dinucleotide.
21. The composition of claim 20 wherein the dinucleotide is CpG.
22. The composition of claim 18, wherein the adjuvant is encoded by a polynucleotide.
23. The composition of claim 18 wherein the adjuvant is a cytokine.
24. The composition of claim 23 wherein the cytokine is GM-CSF.
25. The composition of claim 18 further comprising a professional antigen-presenting cell (pAPC).
26. The composition of claim 25, wherein the pAPC is a dendritic cell.
27. The composition of claim 18, further comprising a second epitope.
28. The composition of claim 27, wherein the second epitope is a polypeptide.
29. The composition of claim 27, wherein the second epitope is a nucleic acid.
30. The composition of claim 27, wherein the second epitope is a housekeeping epitope.
31. The composition of claim 27, wherein the second epitope is an immune epitope.
32. A composition comprising the nucleic acid of claim 1 and a pharmaceutically acceptable adjuvant, carrier, diluent, or excipient.
33. A recombinant construct comprising the nucleic acid of Claim 1.
34. The construct of claim 33, further comprising a plasmid, a viral vector, a bacterial vector, or an artificial chromosome.
35. The construct of claim 33, further comprising a sequence encoding at least one feature selected from the group consisting of a second epitope, an IRES, an ISS, an NIS, and ubiquitin.
36. A purified antibody that specifically binds to the polypeptide of claim 1.
37. A purified antibody that specifically binds to a peptide-MHC protein complex comprising the polypeptide of claim 1.
38. The antibody of claim 36 or claim 37, wherein the antibody is a monoclonal antibody.
39. A multimeric MHC-peptide complex comprising the polypeptide of claim 1.
40. An isolated T cell expressing a T cell receptor specific for an MHC-peptide complex, the complex comprising the polypeptide of claim 1.
41. The T cell of claim 40, produced by an *in vitro* immunization.
42. The T cell of claim 40, isolated from an immunized animal.
43. A T cell clone comprising the T cell of claim 40.

44. A polyclonal population of T cells comprising the T cell of claim 40.
45. A pharmaceutical composition comprising the T cell of claim 40 and a pharmaceutically acceptable adjuvant, carrier, diluent, or excipient.
46. An isolated protein molecule comprising the binding domain of a T cell receptor specific for an MHC-peptide complex, the complex comprising the epitope of claim 1.
47. The protein of claim 46, wherein the protein is multivalent.
48. An isolated nucleic acid encoding the protein of claim 46.
49. A recombinant construct comprising the nucleic acid of claim 48.
50. A host cell expressing a recombinant construct, the construct comprising the nucleic acid of claim 1, or the construct encoding a protein molecule comprising the binding domain of a T cell receptor specific for an MHC-peptide complex.
51. The host cell of claim 50, wherein the host cell is a dendritic cell, macrophage, tumor cell, or tumor-derived cell.
52. The host cell of claim 50, wherein the host cell is a bacterium, fungus, or protozoan.
53. A composition comprising the host cell of claim 50 and a pharmaceutically acceptable adjuvant, carrier, diluent, or excipient.
54. A composition comprising at least one component selected from the group consisting of the epitope of claim 1; the composition of claim 18, 32, or 45, the construct of claim 33; the T cell of claim 40, a host cell expressing a recombinant construct comprising a nucleic acid encoding a T cell receptor binding domain specific for an MHC-peptide complex and a composition comprising the same, and a host cell expressing a recombinant construct comprising the nucleic acid of claim 1 and a composition comprising the same.
55. A method of treating an animal, comprising:
administering to an animal the composition of claim 54.
56. The method of claim 55, wherein the administering step comprises a mode of delivery selected from the group consisting of transdermal, intranodal, perinodal, oral, intravenous, intradermal, intramuscular, intraperitoneal, mucosal, aerosol inhalation, and instillation.
57. The method of claim 55, further comprising a step of assaying to determine a characteristic indicative of a state of a target cell or target cells.
58. The method of claim 57, comprising a first assaying step and a second assaying step, wherein the first assaying step precedes the administering step, and wherein the second assaying step follows the administering step.
59. The method of claim 58, further comprising a step of comparing the characteristic determined in the first assaying step with the characteristic determined in the second assaying step to obtain a result.

60. The method of claim 59, wherein the result is selected from the group consisting of: evidence of an immune response, a diminution in number of target cells, a loss of mass or size of a tumor comprising target cells, a decrease in number or concentration of an intracellular parasite infecting target cells.

61. A method of evaluating immunogenicity of an immunogenic composition, comprising:

administering to an animal the composition of claim 54; and
evaluating immunogenicity based on a characteristic of the animal.

62. The method of claim 61, wherein the animal is MHC-transgenic.

63. A method of evaluating immunogenicity, comprising:

in vitro stimulation of a T cell with the composition of claim 54; and
evaluating immunogenicity based on a characteristic of the T cell.

64. The method of claim 63, wherein the stimulation is a primary stimulation.

65. A method of making a passive/adoptive immunotherapeutic, comprising:

combining the T cell of claim 40, or a host cell expressing a recombinant construct comprising a nucleic acid encoding a T cell receptor binding domain specific for an MHC-peptide complex, or a host cell expressing a recombinant construct comprising the nucleic acid of claim 1 with a pharmaceutically acceptable adjuvant, carrier, diluent, or excipient.

66. A method of determining specific T cell frequency comprising the step of contacting T cells with a MHC-peptide complex comprising the polypeptide of claim 1.

67. The method of claim 66, wherein the contacting step comprises at least one feature selected from the group consisting of immunization, restimulation, detection, and enumeration.

68. The method of Claim 66, further comprising ELISPOT analysis, limiting dilution analysis, flow cytometry, in situ hybridization, the polymerase chain reaction or any combination thereof.

69. A method of evaluating immunologic response, comprising the method of claim 66 carried out prior to and subsequent to an immunization step.

70. A method of evaluating immunologic response, comprising:

determining frequency, cytokine production, or cytolytic activity of T cells, prior to and subsequent to a step of stimulation with MHC-peptide complexes comprising the polypeptide of claim 1.

71. A method of diagnosing a disease comprising:

contacting a subject tissue with at least one component selected from the group consisting of the T cell of claim 40, the host cell of claim 50, the antibody of claim 36, and the protein of claim 46; and

diagnosing the disease based on a characteristic of the tissue or of the component.

72. The method of claim 71, wherein the contacting step takes place *in vivo*.

73. The method of claim 71, wherein the contacting step takes place *in vitro*.

74. A method of making a vaccine, comprising:

combining at least one component selected from the group consisting of the polypeptide of claim 1; the composition of claim 18, 32, 45, or 53; the construct of claim 33; the T cell of claim 40, and the host cell of claim 50, with a pharmaceutically acceptable adjuvant, carrier, diluent, or excipient.

75. A computer readable medium having recorded thereon the sequence of any one of SEQ ID NOS: 108-610, in a machine having a hardware or software that calculates the physical, biochemical, immunologic, or molecular genetic properties of a molecule embodying said sequence.

76. A method of treating an animal comprising combining the method of claim 55 combined with at least one mode of treatment selected from the group of radiation therapy, chemotherapy, biochemotherapy, and surgery.

77. An isolated polypeptide comprising an epitope cluster from a target-associated antigen having the sequence as disclosed in Tables 68-73, wherein the amino acid sequence consists of not more than about 80% of the amino acid sequence of the antigen.

78. A vaccine or immunotherapeutic product comprising the polypeptide of claim 77.

79. An isolated polynucleotide encoding the polypeptide of claim 77.

80. A vaccine or immunotherapeutic product comprising the polynucleotide of claim 79.

81. The polynucleotide of claim 79 or 80, wherein the polynucleotide is DNA.

82. The polynucleotide of claim 79 or 80, wherein the polynucleotide is RNA.

FIG. 1B

| | | | |
|--------------------|-------|-------------------|-------------------------|
| | | 101 | 150 |
| CTAG_HUMAN NY-ESO | (101) | EAELVRRILSRDAAPLP | REGAGRMRV |
| AA05202 - CAG-3 | (101) | EAELVRRILSRDAAPLP | REGAGRMRV |
| CAA11044 -LAGE-1a | (101) | EAELVRRILSRDAAPLP | REGAGRMRV |
| CAA10194 - LAGE-1s | (101) | EAELVRRILSRDAAPLP | REGAGRMRV |
| CAA11043 - LAGE-1b | (101) | EAELVRRILSRDAAPLP | REGAGRMRV |
| CAA10196 - LAGE-1L | (101) | EAELVRRILSRDAAPLP | REGAGRMRV |
| AAH02833 CT-2 | (101) | EAELVRRILSRDAAPLP | REGAGRMRV |
| Consensus | (101) | EAELVRRILSRDAAPLP | REGAGRMRV |
| | | 151 | 200 |
| CTAG_HUMAN NY-ESO | (151) | VGWGLGASPEGQKARDL | TPGTPGPPPPPEGAQGDGCRGVA |
| AA05202 - CAG-3 | (151) | VGWGLGASPEGQKARDL | TPGTPGPPPPPEGAQGDGCRGVA |
| CAA11044 -LAGE-1a | (151) | VGWGLGASPEGQKARDL | TPGTPGPPPPPEGAQGDGCRGVA |
| CAA10194 - LAGE-1s | (151) | VGWGLGASPEGQKARDL | TPGTPGPPPPPEGAQGDGCRGVA |
| CAA11043 - LAGE-1b | (151) | VGWGLGASPEGQKARDL | TPGTPGPPPPPEGAQGDGCRGVA |
| CAA10196 - LAGE-1L | (151) | VGWGLGASPEGQKARDL | TPGTPGPPPPPEGAQGDGCRGVA |
| AAH02833 CT-2 | (151) | VGWGLGASPEGQKARDL | TPGTPGPPPPPEGAQGDGCRGVA |
| Consensus | (151) | VGWGLGASPEGQKARDL | TPGTPGPPPPPEGAQGDGCRGVA |

FIG. 1C

| | | |
|--------------------|-------|-----------|
| | 201 | |
| CTAG_HUMAN NY-ESO | (181) | ----- |
| AAD05202 - CAG-3 | (181) | ----- |
| CAA11044 -LAGE-1a | (181) | ----- |
| CAA10194 - LAGE-1s | (181) | ----- |
| CAA11043 - LAGE-1b | (201) | ENVMSAPHI |
| CAA10196 - LAGE-1L | (201) | ENVMSAPHI |
| AAH02833 CT-2 | (201) | ENVMSAPHI |
| Consensus | (201) | |

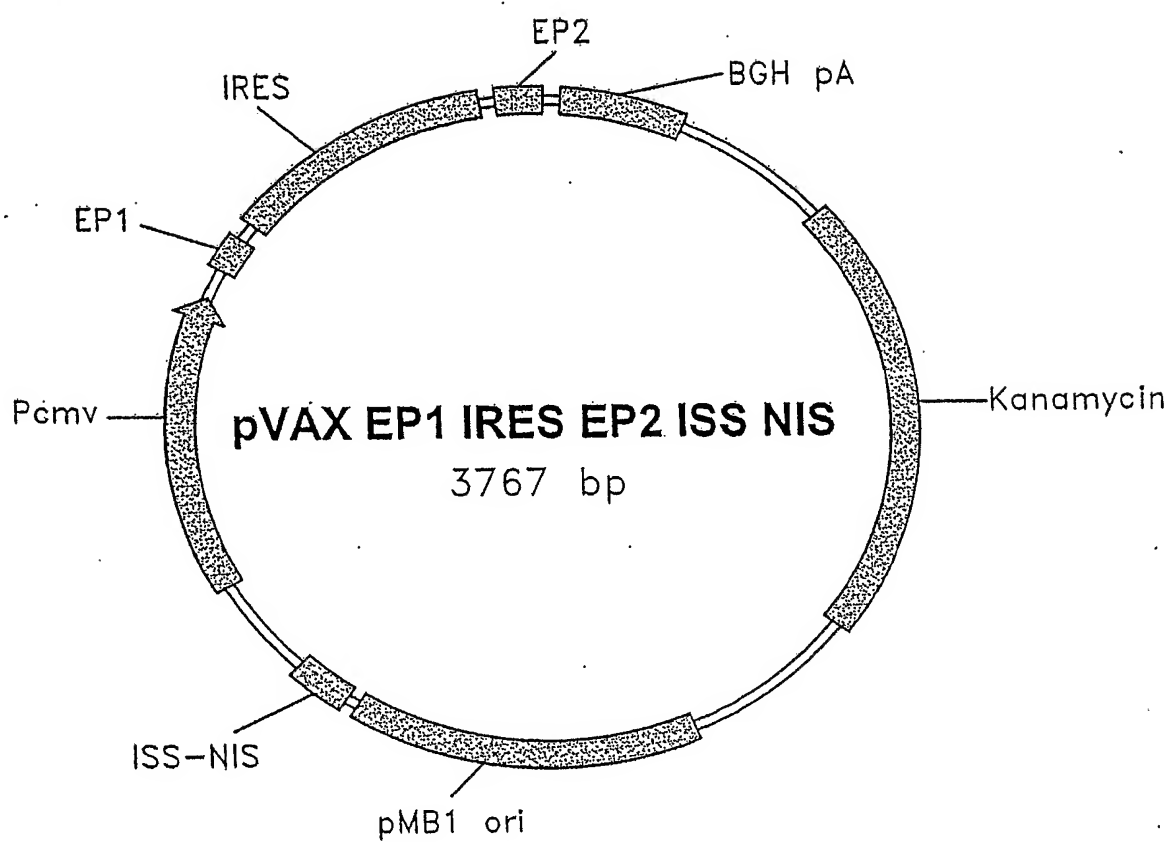
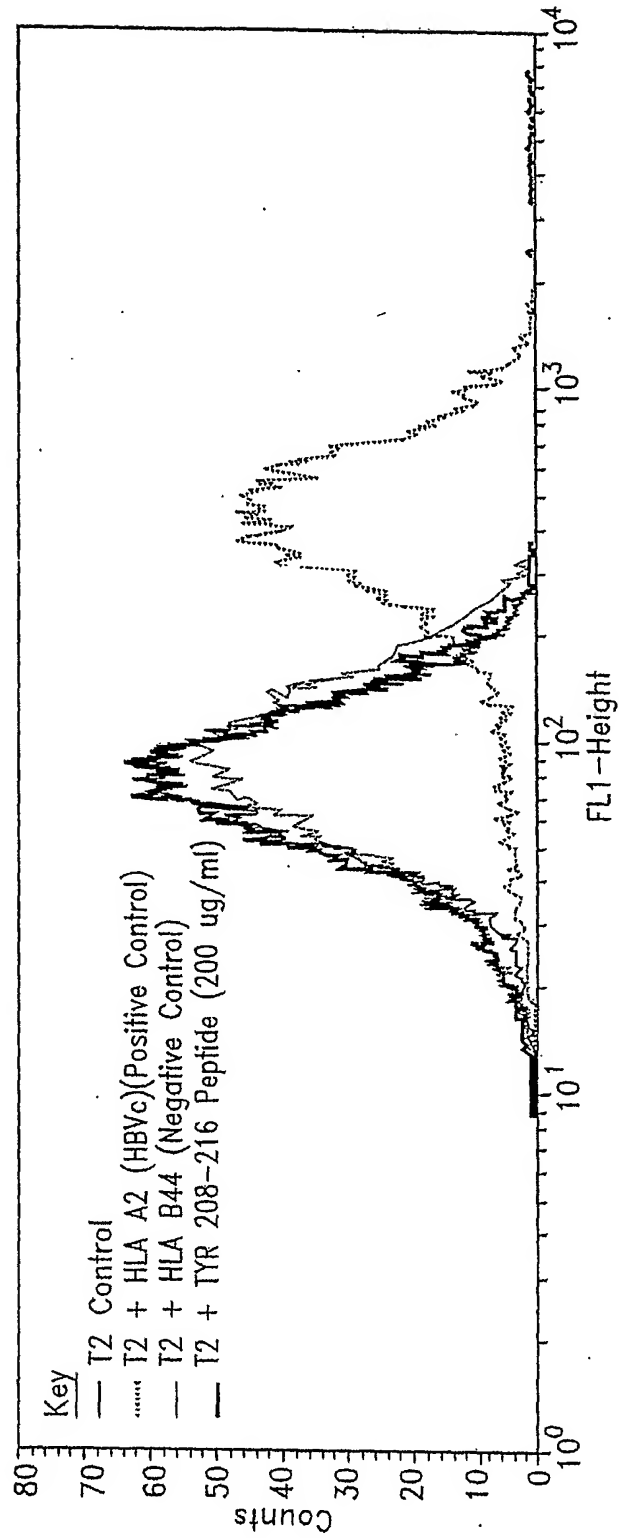


FIG. 2

FIG. 3A

**FACscan Analysis of Binding Assay to Determine the Binding
Ability of Tyrosinase 208-216 Peptide to MHC Class 1**

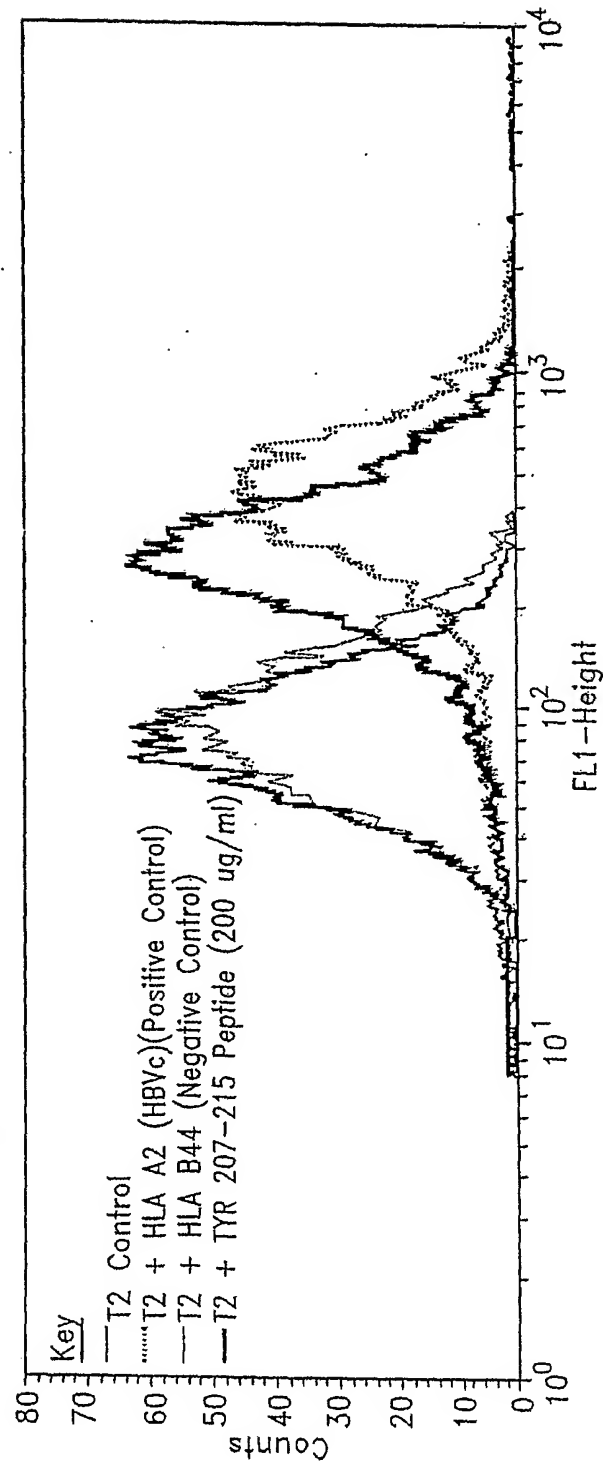


F1 (HLA A2 Peptide) = 3.13

F1 (TYR 208-216 Peptide) = 0.01

FIG. 3B

**FACScan Analysis of Binding Assay to Determine the Binding
Ability of Tyrosinase 207-215 Peptide to MHC Class 1**

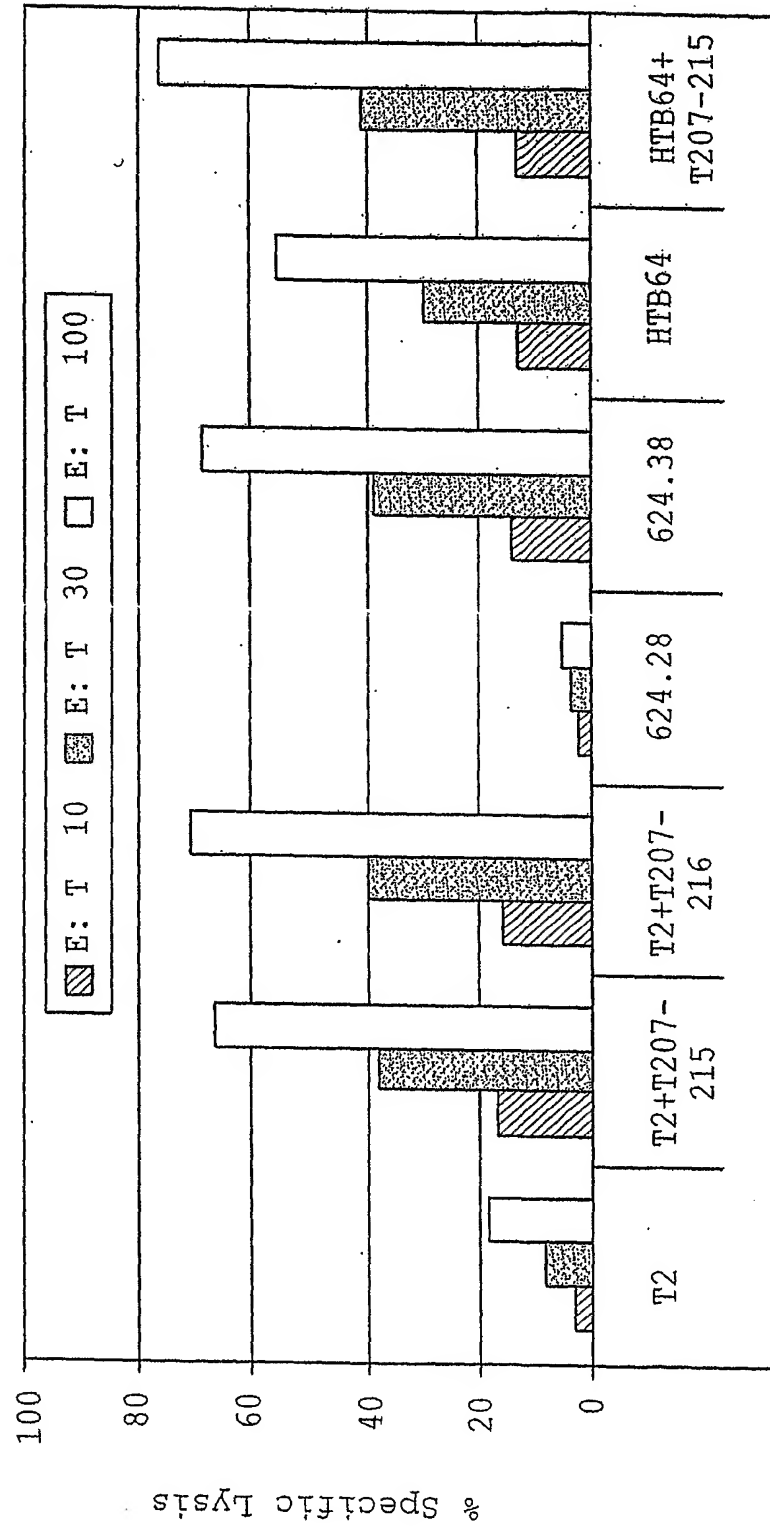


F1 (HLA A2 Peptide) = 3.13

F1 (TYR 207-215 Peptide) = 2.00

FIG. 3C

HLA A2 restricted and tyrosinase specific lysis by CTL from Tyr207-215 IVS blood



CTL from Tyr 207-215 IVS blood

FIG. 4

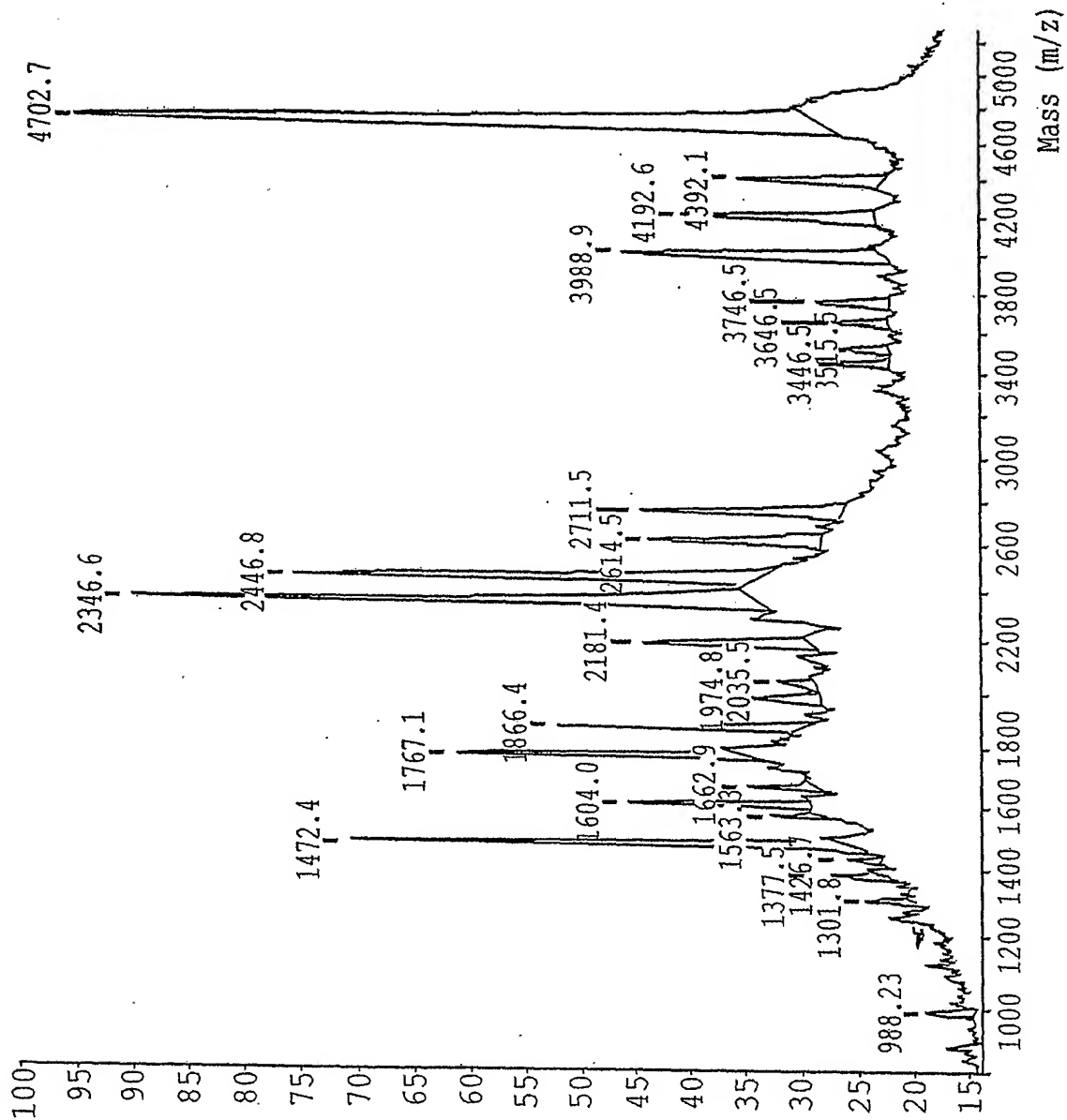


FIG. 5
Comparison of Peptides Binding Affinity to HLA A2.

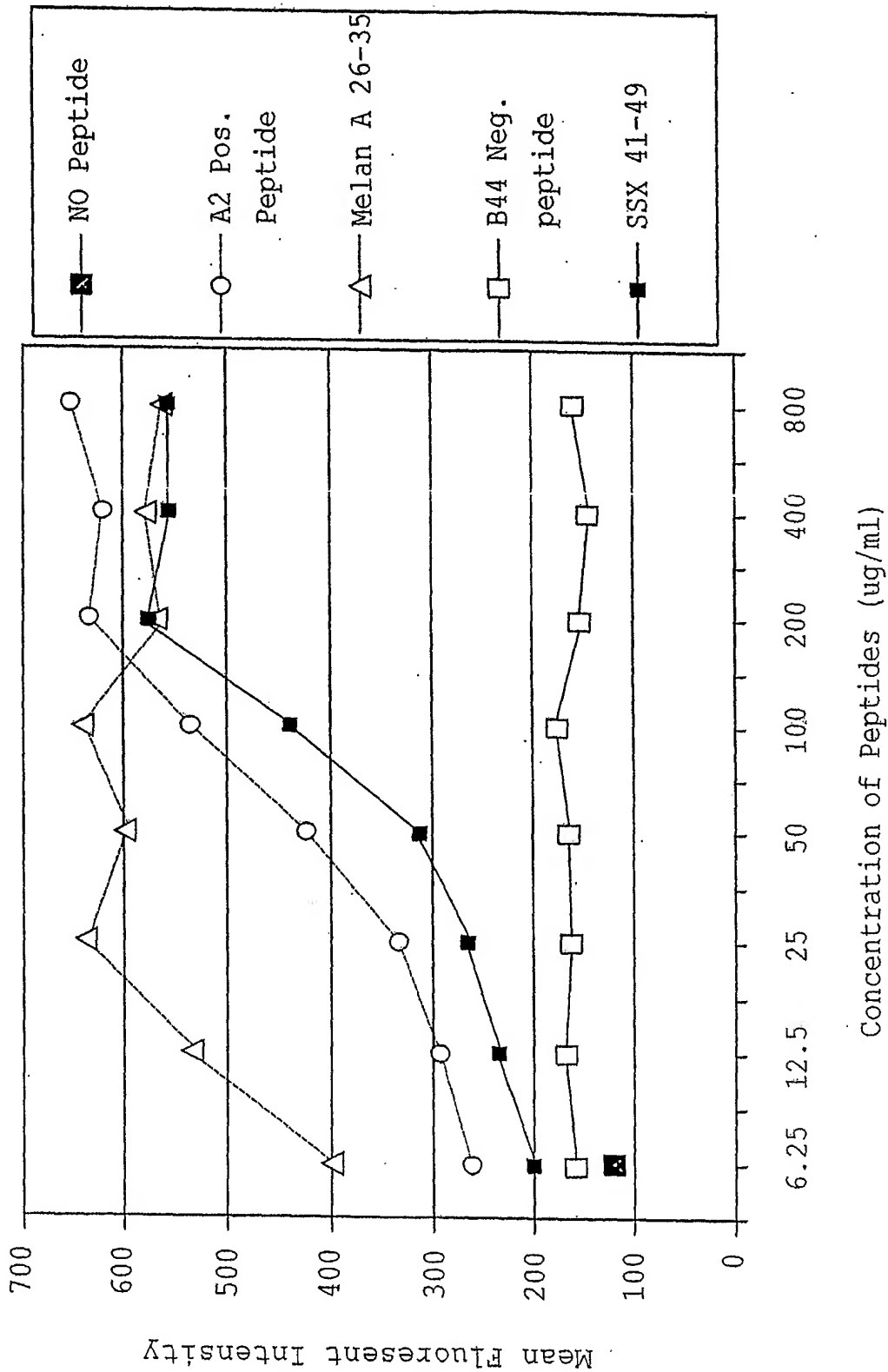


FIG. 6

SSX2₄₁₋₄₉ specific lysis by CTL from peptide injected HHD1 mice

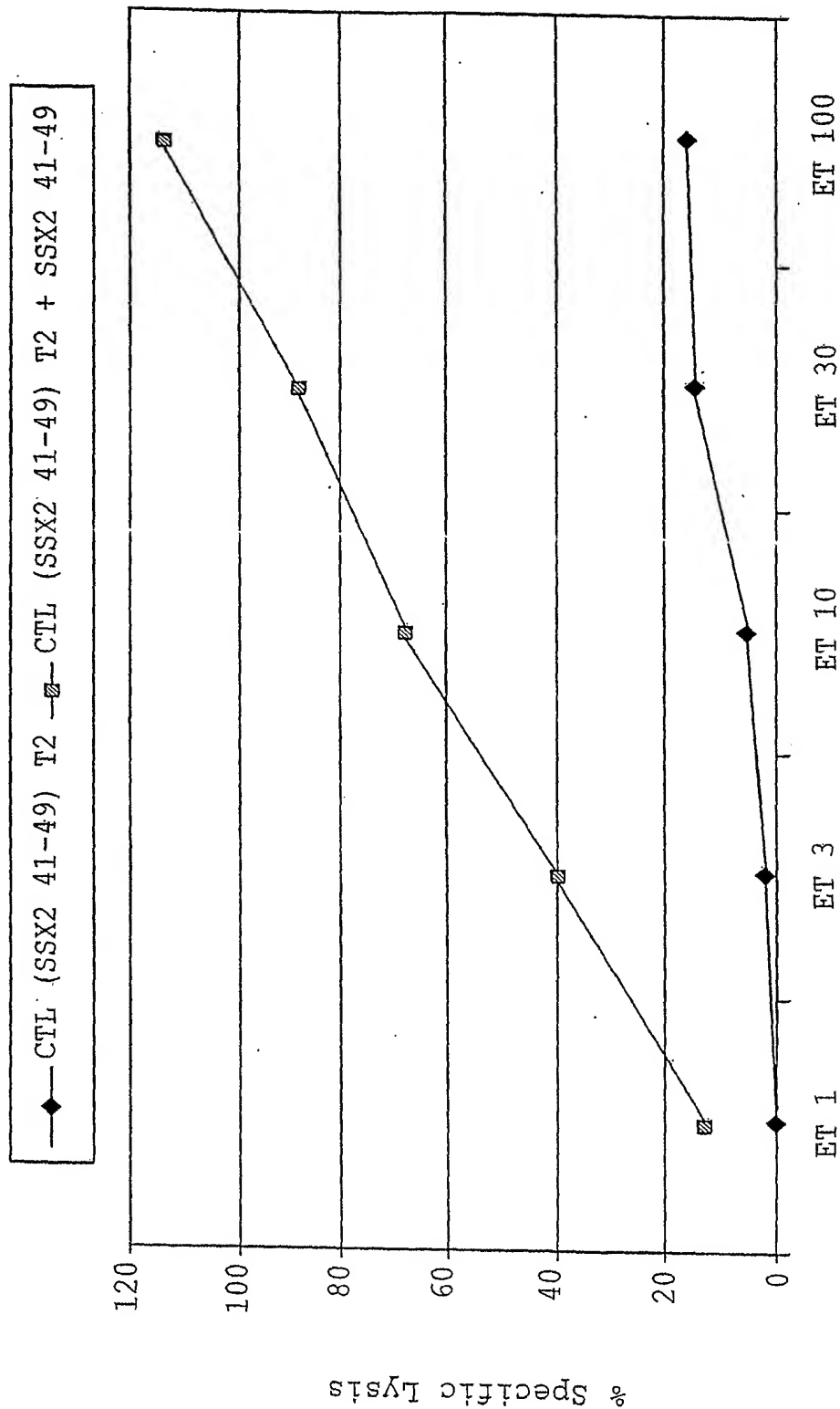
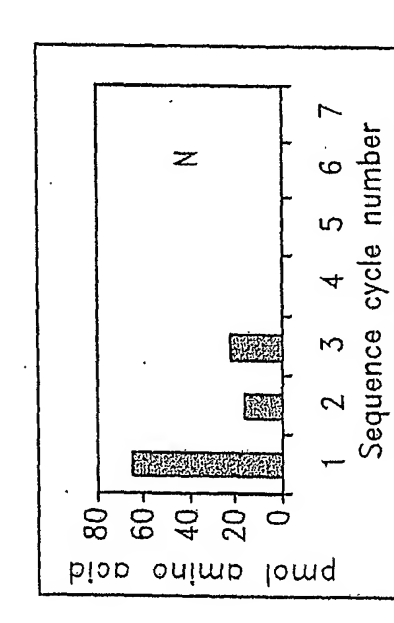
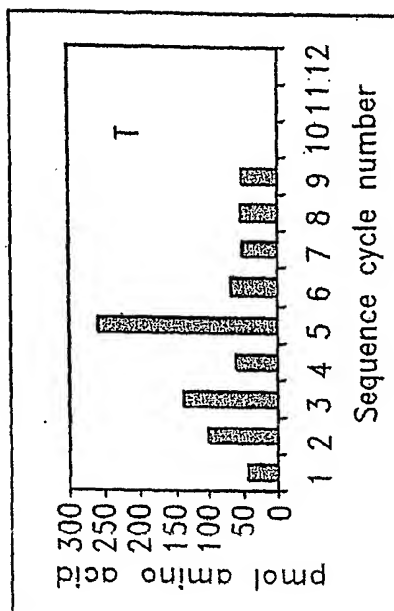
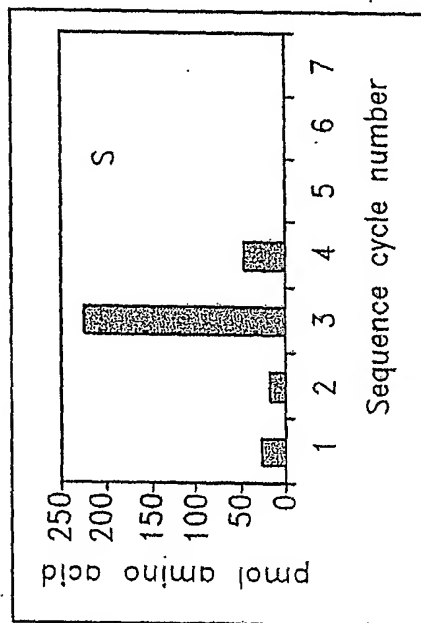
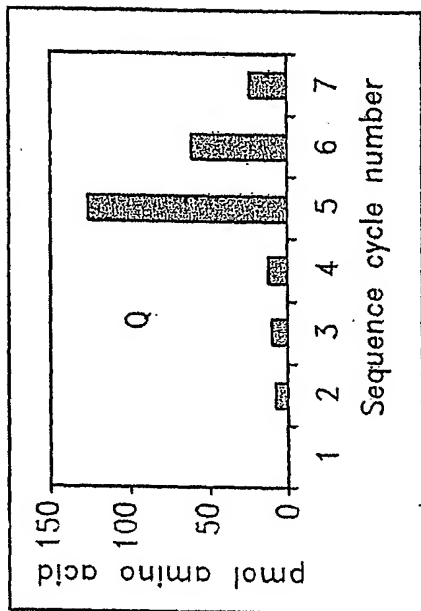


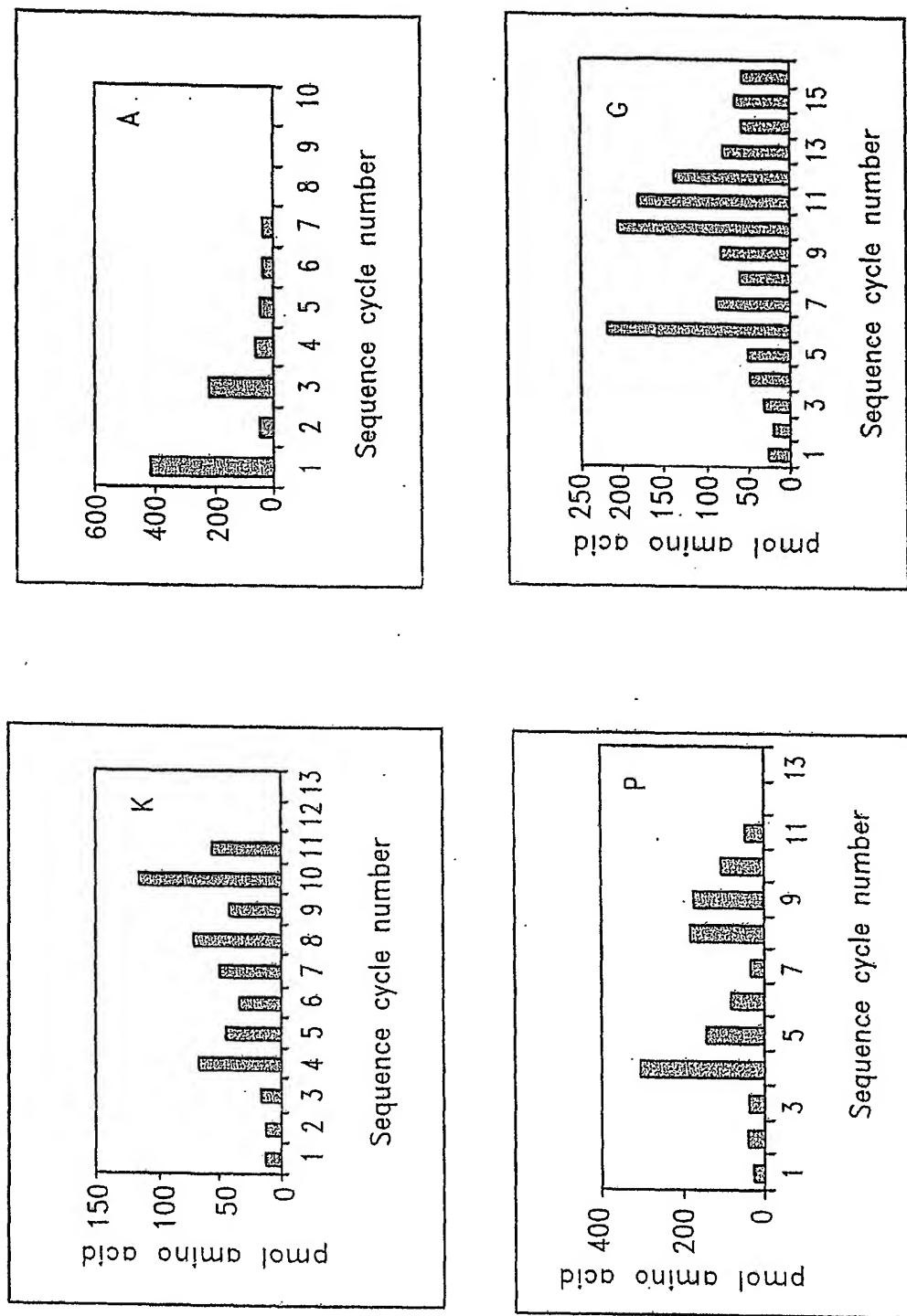
FIG. 7A

163-AFSPQGMPEGLVYV**N**YARTEDEFFKLERDM-192

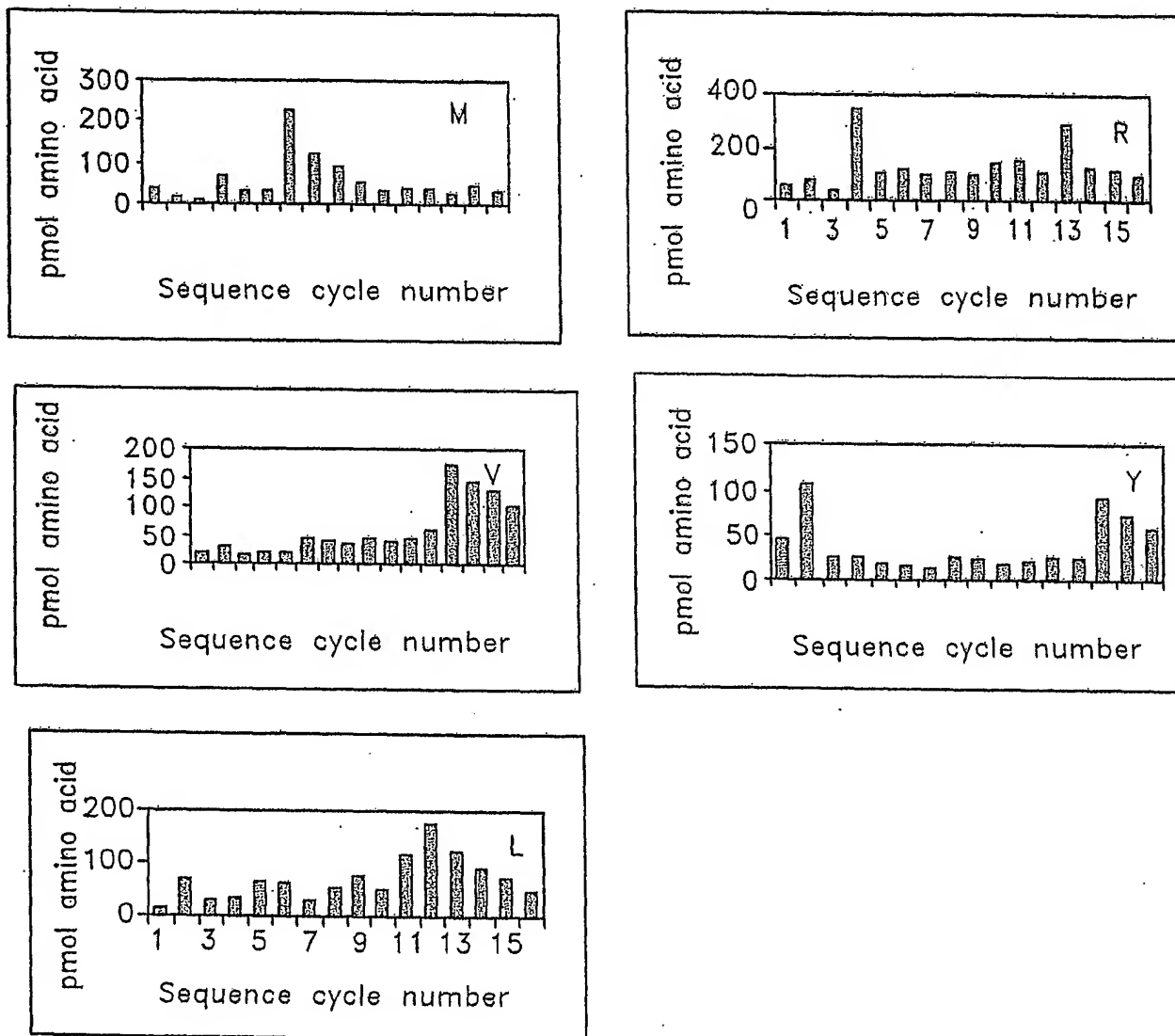


Pool sequencing of PSMA_163-192 Digested for 60 min by proteasome

FIG. 7B



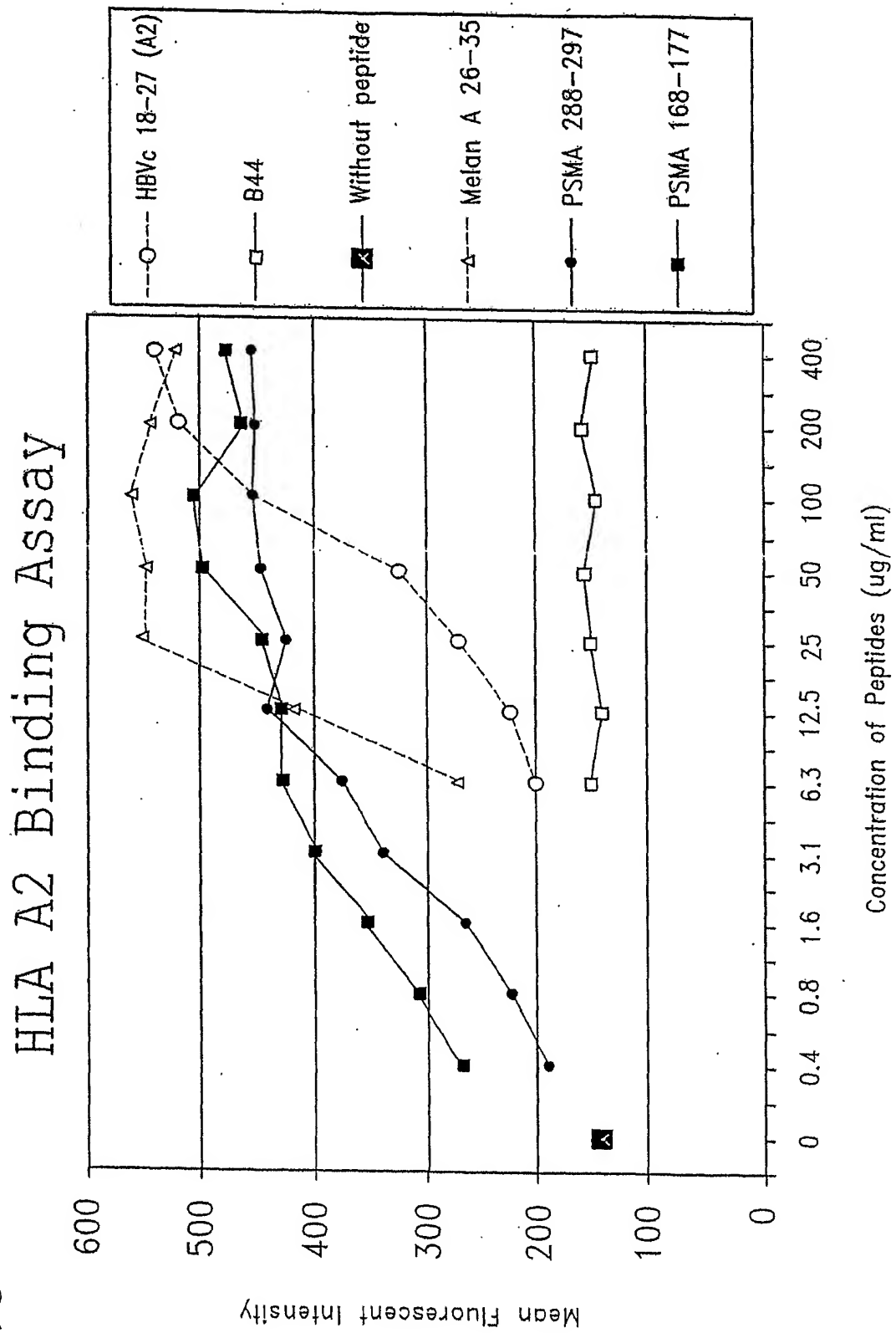
Pool sequencing of PSMA_163-192 Digested for 60 min by proteasome

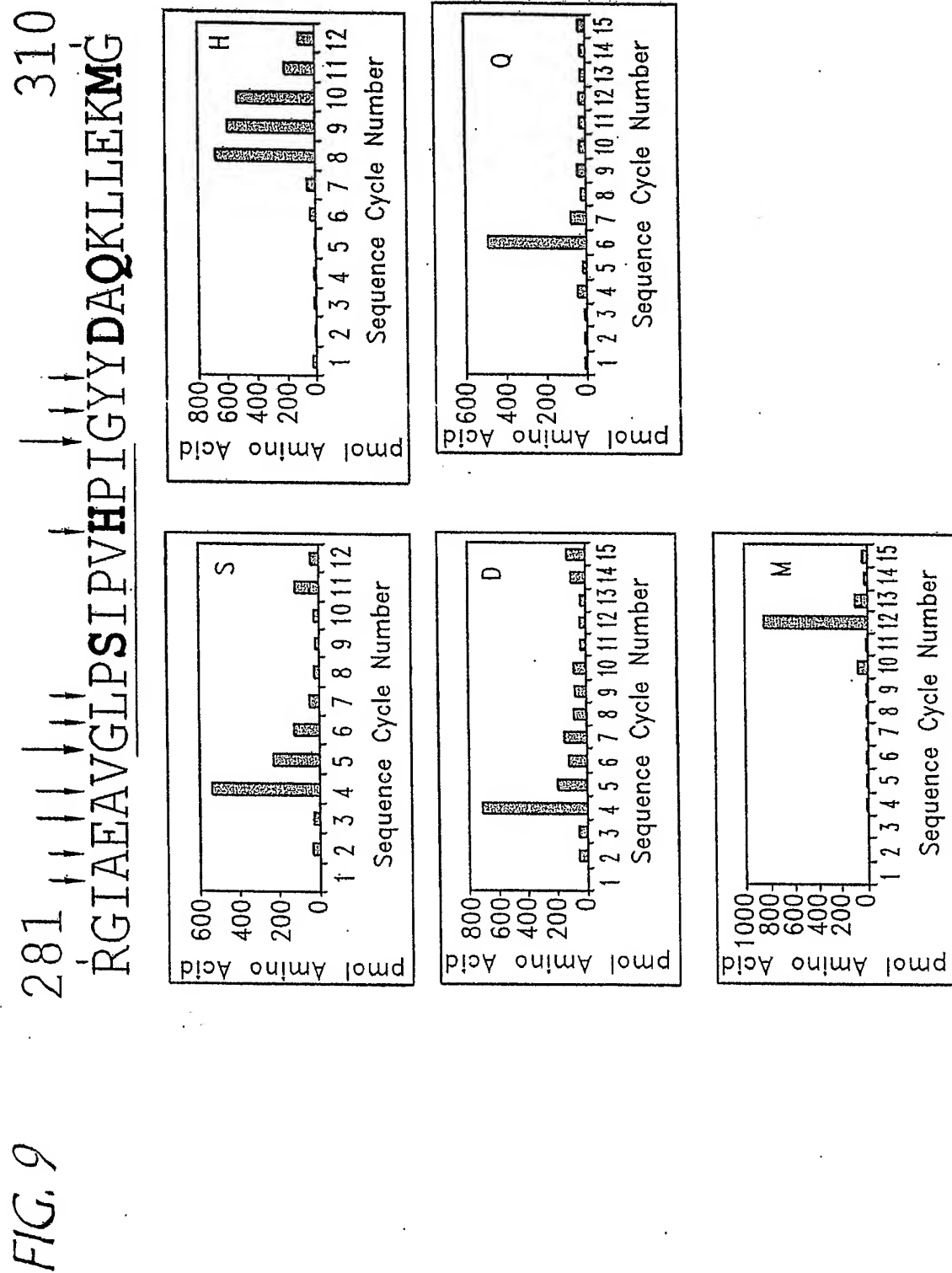


Pool sequencing of PSMA₁₆₃₋₁₉₂ Digested for 60 min by proteasome

FIG. 7C

FIG. 8





Pool sequencing of PSMA_281_310 Digested for 60 min by Proteasome

Autologous DC Present A1 Peptide to CD8 T cell

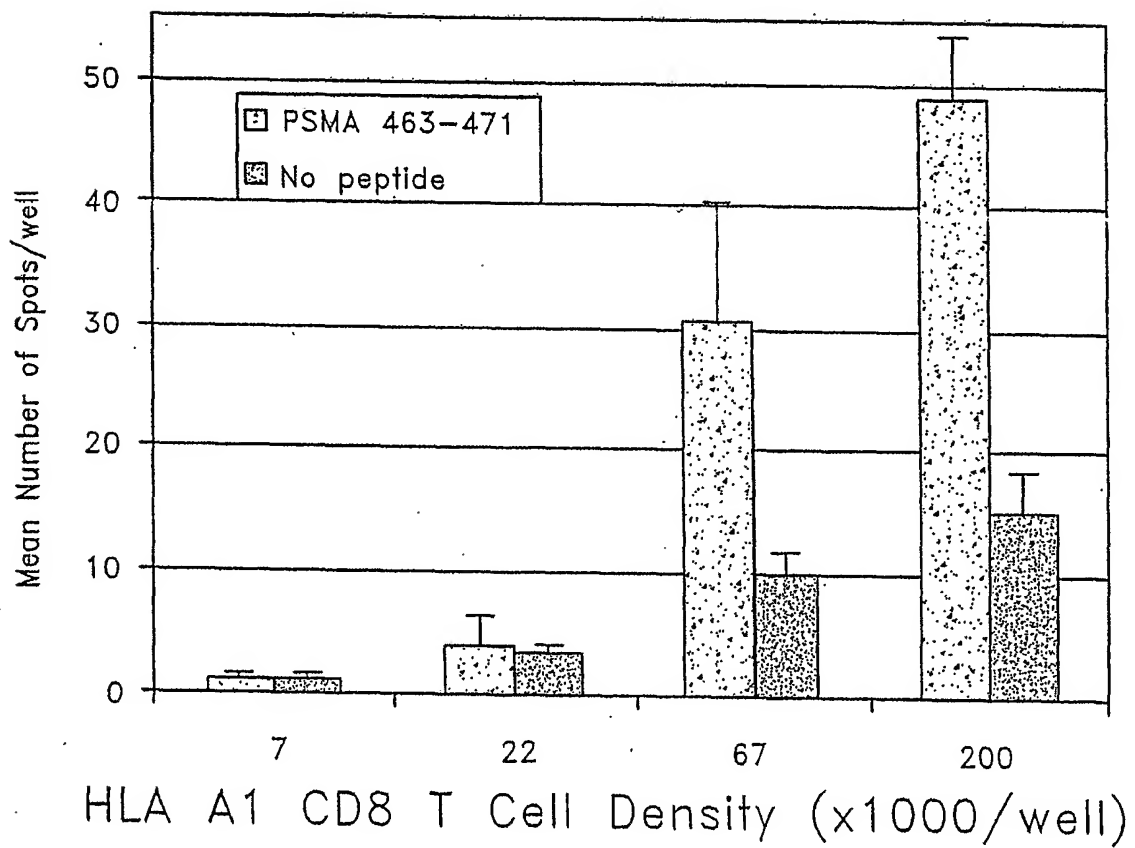


FIG. 11

Secretion of IFN γ Was Blocked by Anti-A1 Antibody

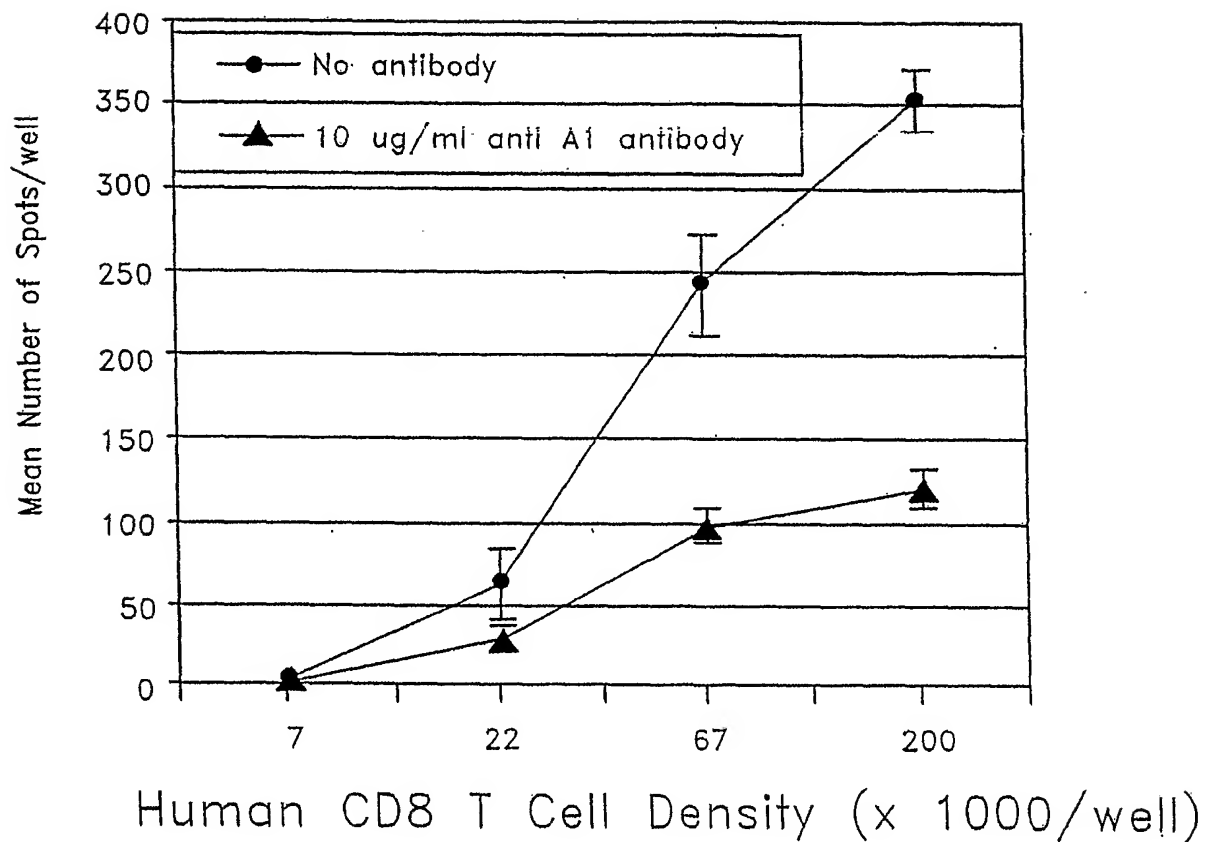


FIG. 12

FIG. 13

Comparison of Peptides Binding Affinity to HLA A2 by Binding Assay

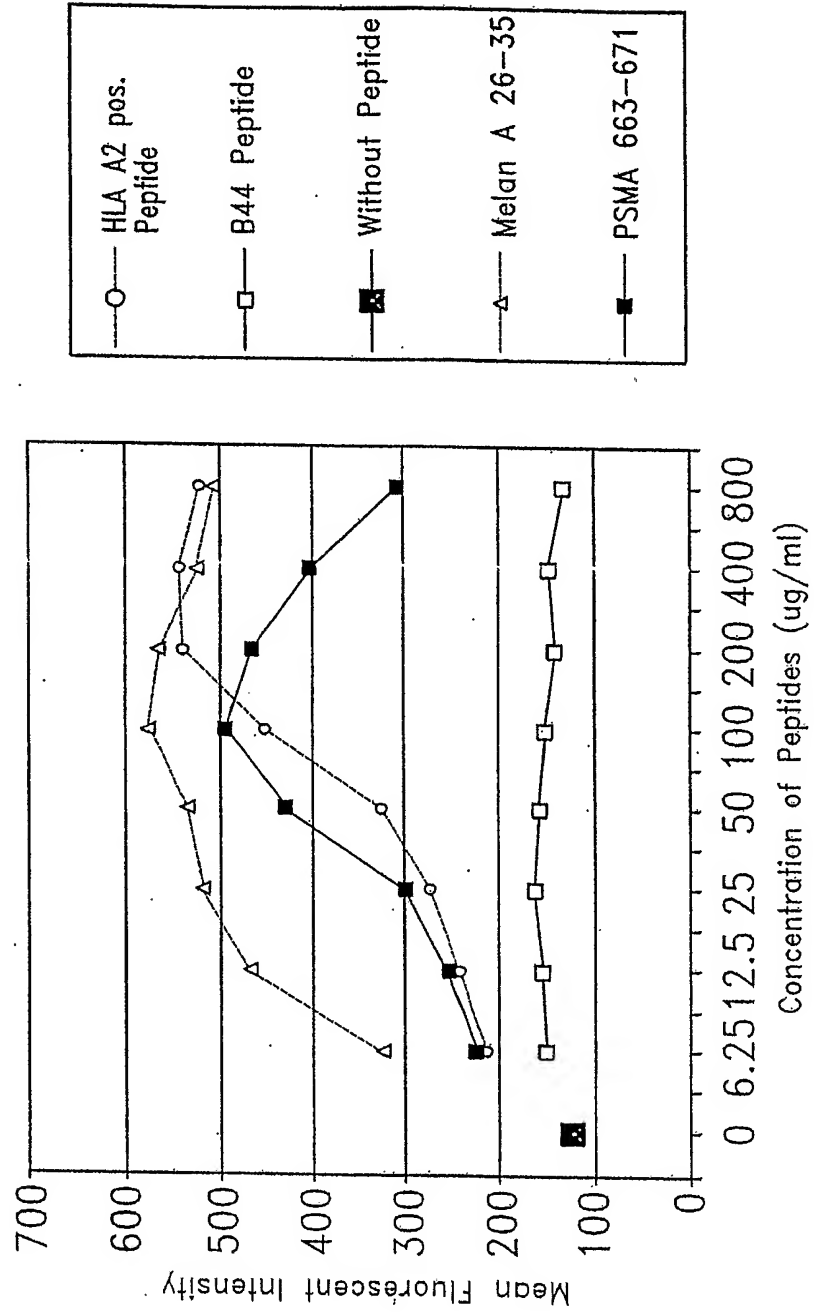
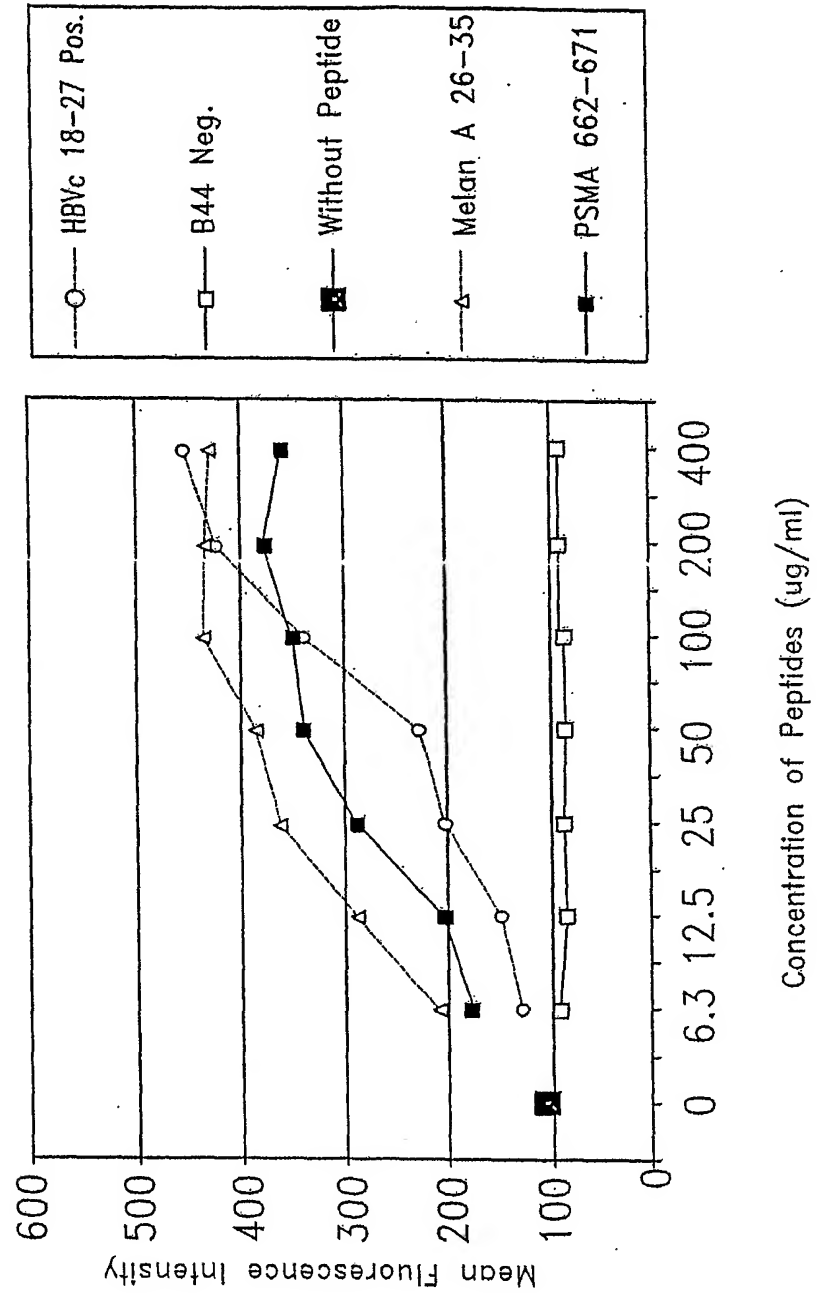
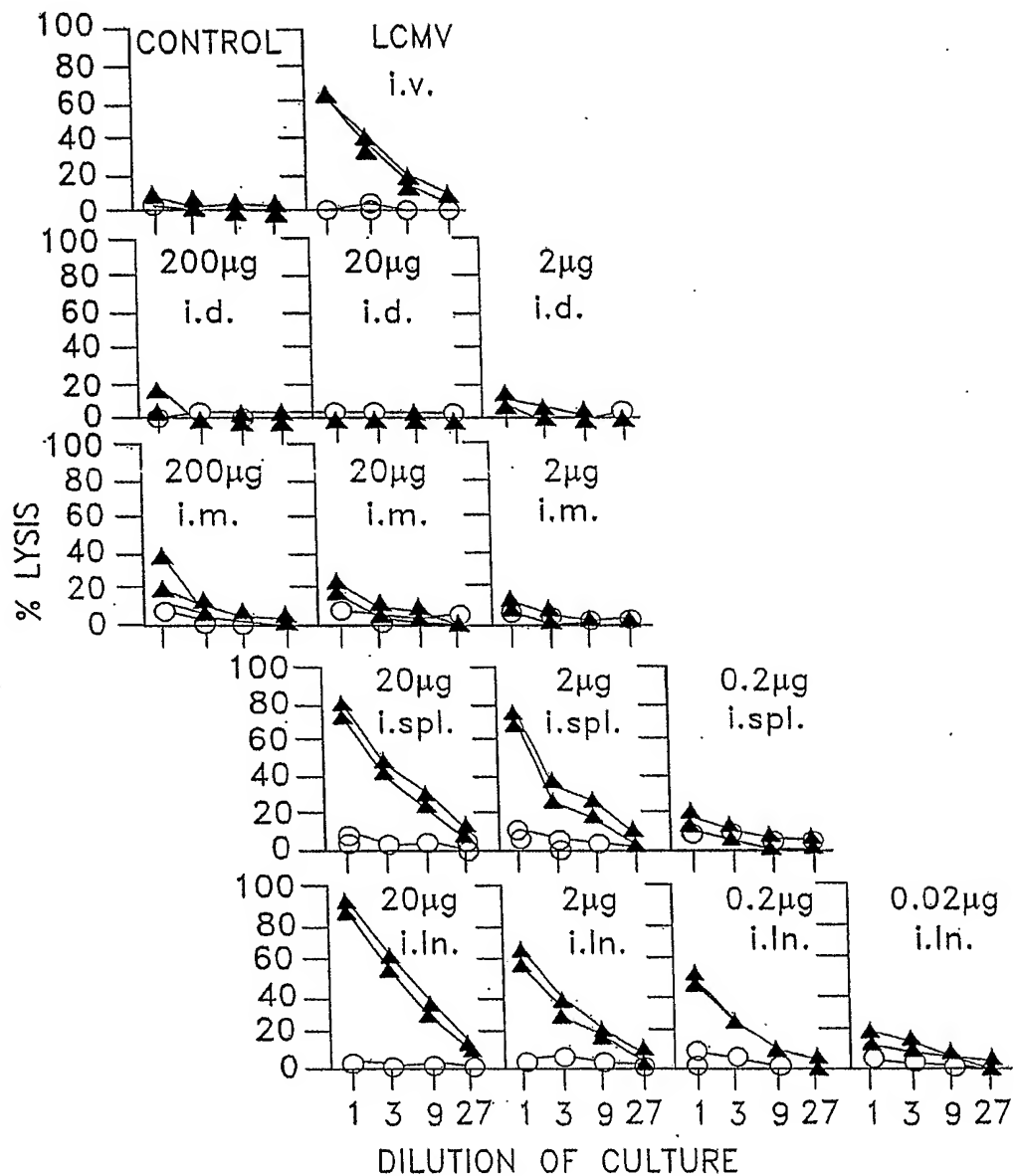


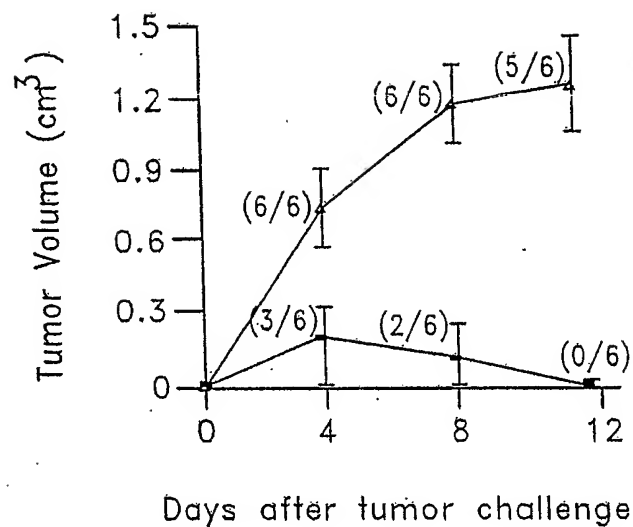
FIG. 14
Comparison of Peptides Binding Affinity
to HLA A2 by Binding Assay





Graphs show lysis of unpulsed EL4 cells (open circles) and EL4 cells pulsed with gp33 peptide (solid triangles). Symbols represent individual mice and one of three similar experiments is shown.

FIG. 15



Mean tumor volumes \pm 1SD are shown for mice immunized with pEFGPL33A DNA (solid circles) or control pEGFP-N3 DNA (open triangles). Numbers in brackets indicate number of mice with tumors/total number of mice in group. One of two similar experiments is shown.

FIG. 16

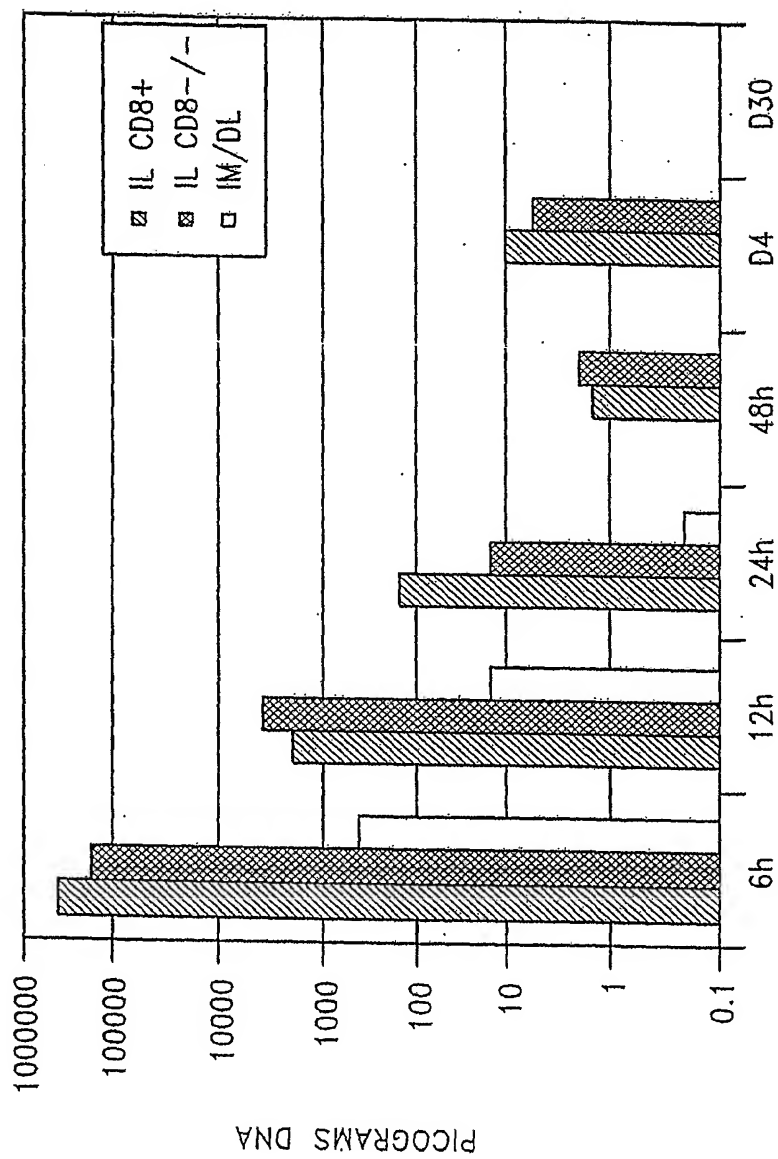


FIG. 17

Tyrosinase (171-203)

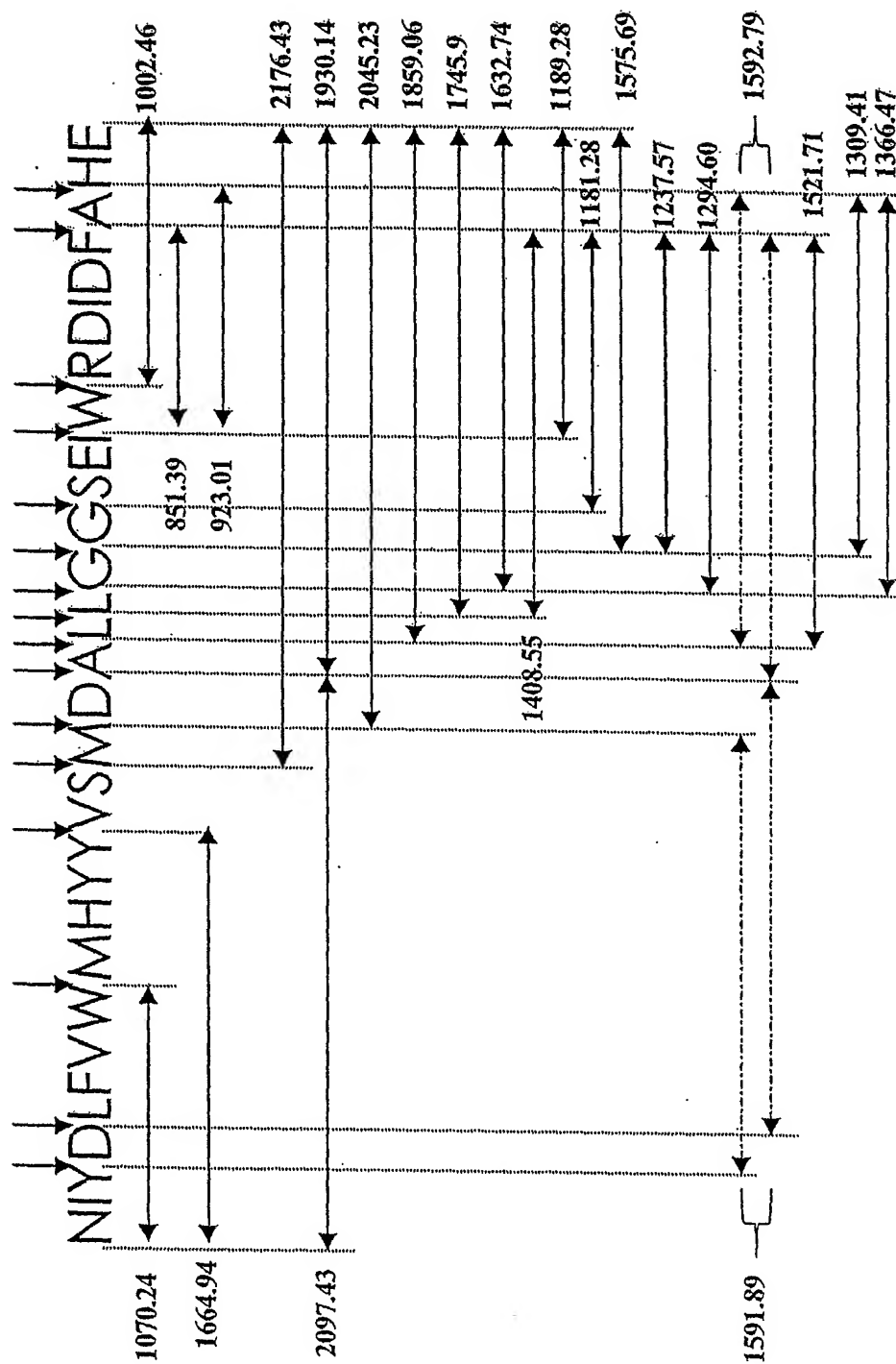


Figure 18

Tyr (401-427)

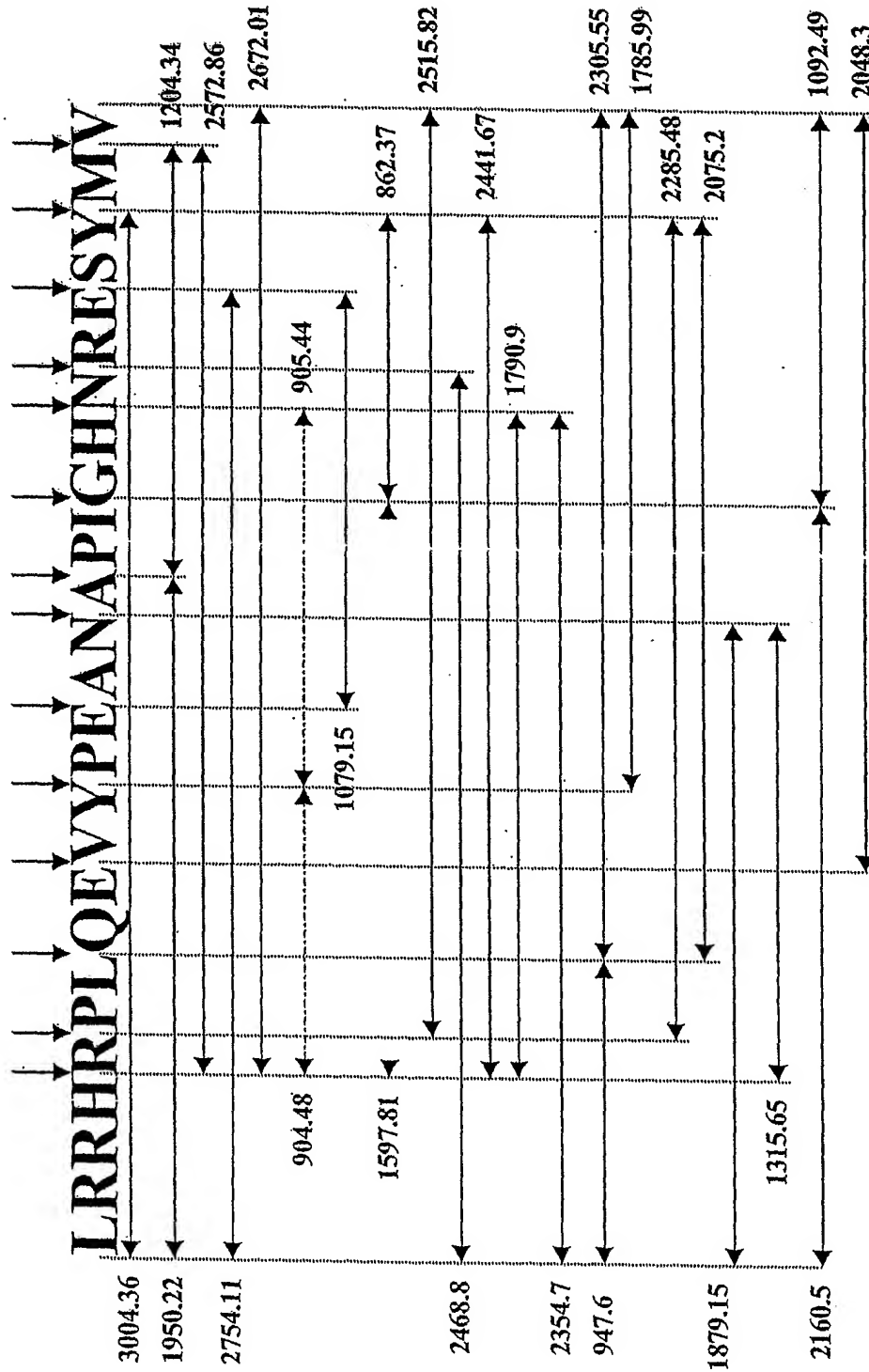


Figure 19

Tyrosinase (415-449)

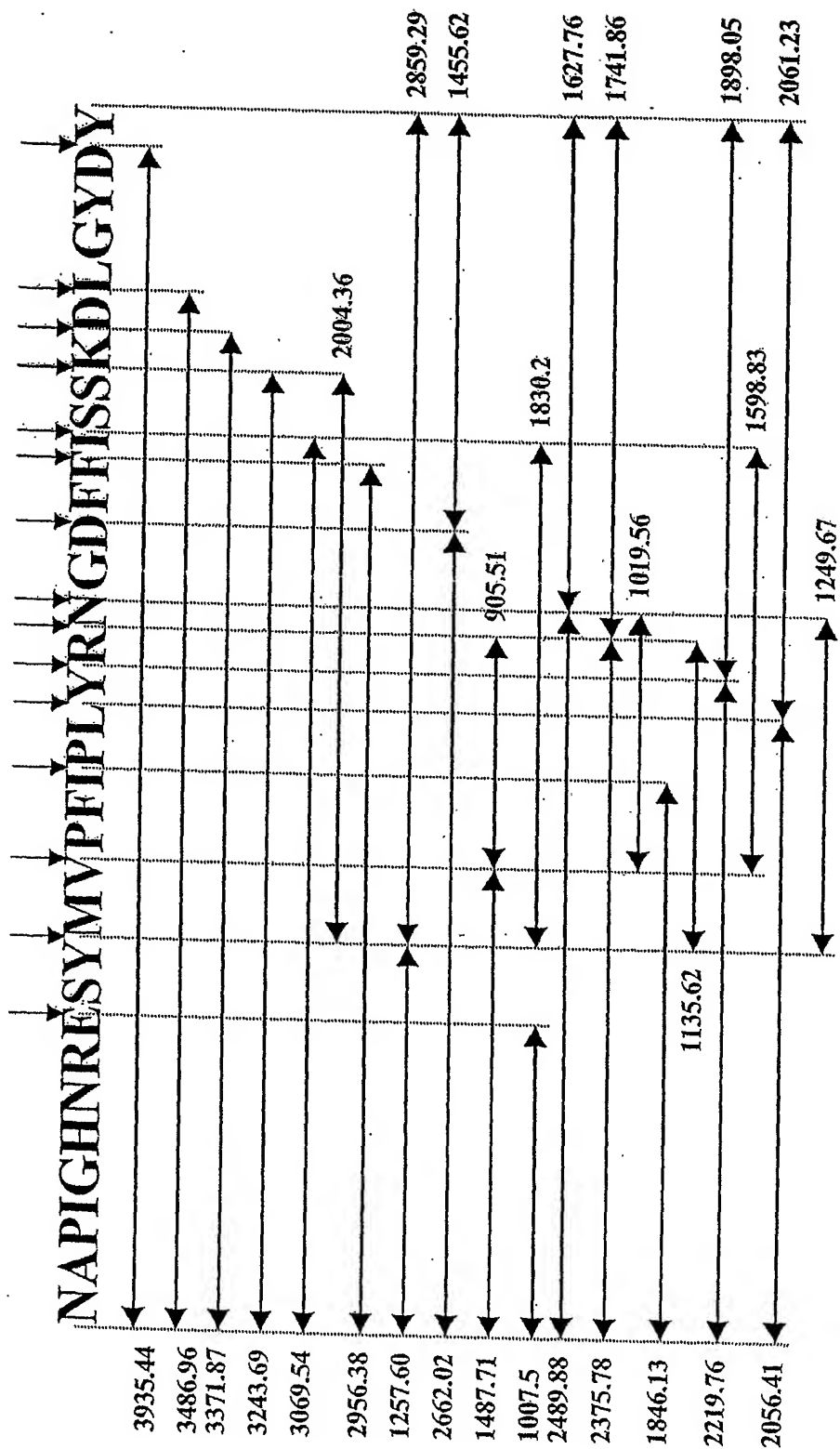


Figure 20

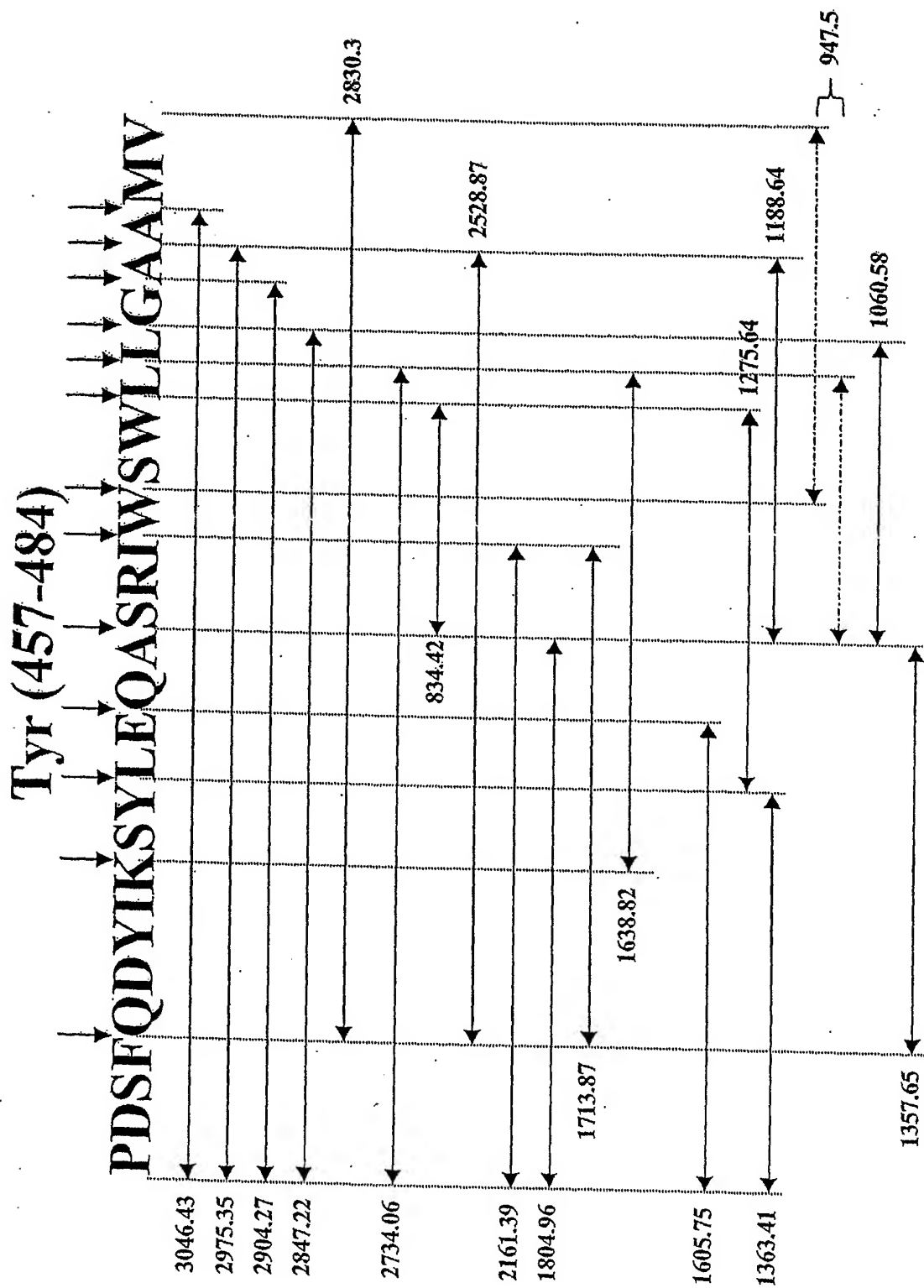


Figure 21

CEA 92-118

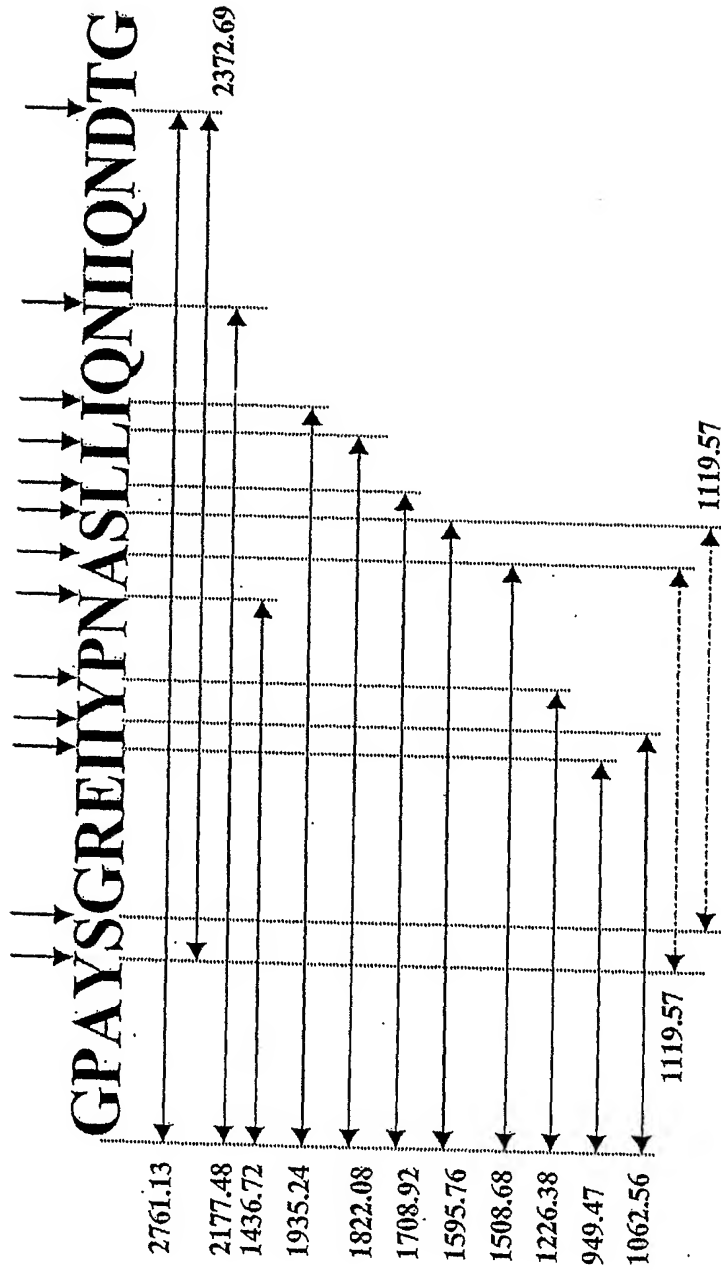


Figure 22

CEA 131-159

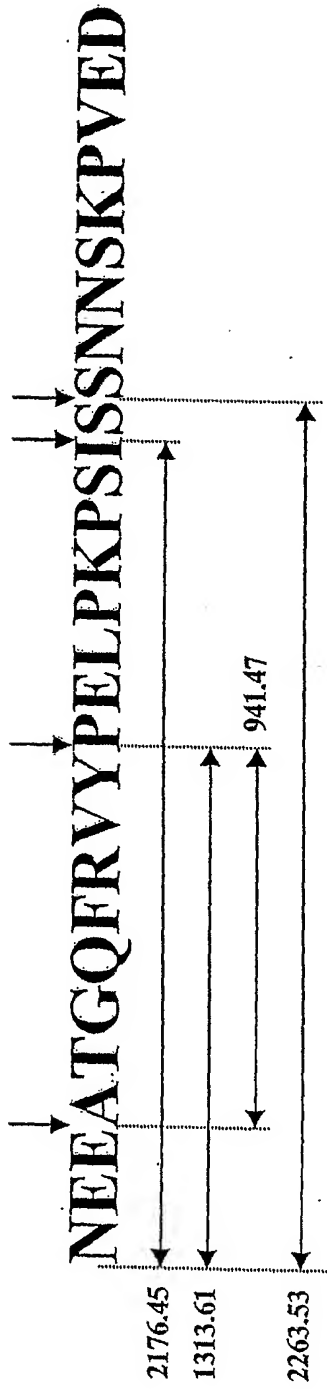


Figure 23

CEA 225-251

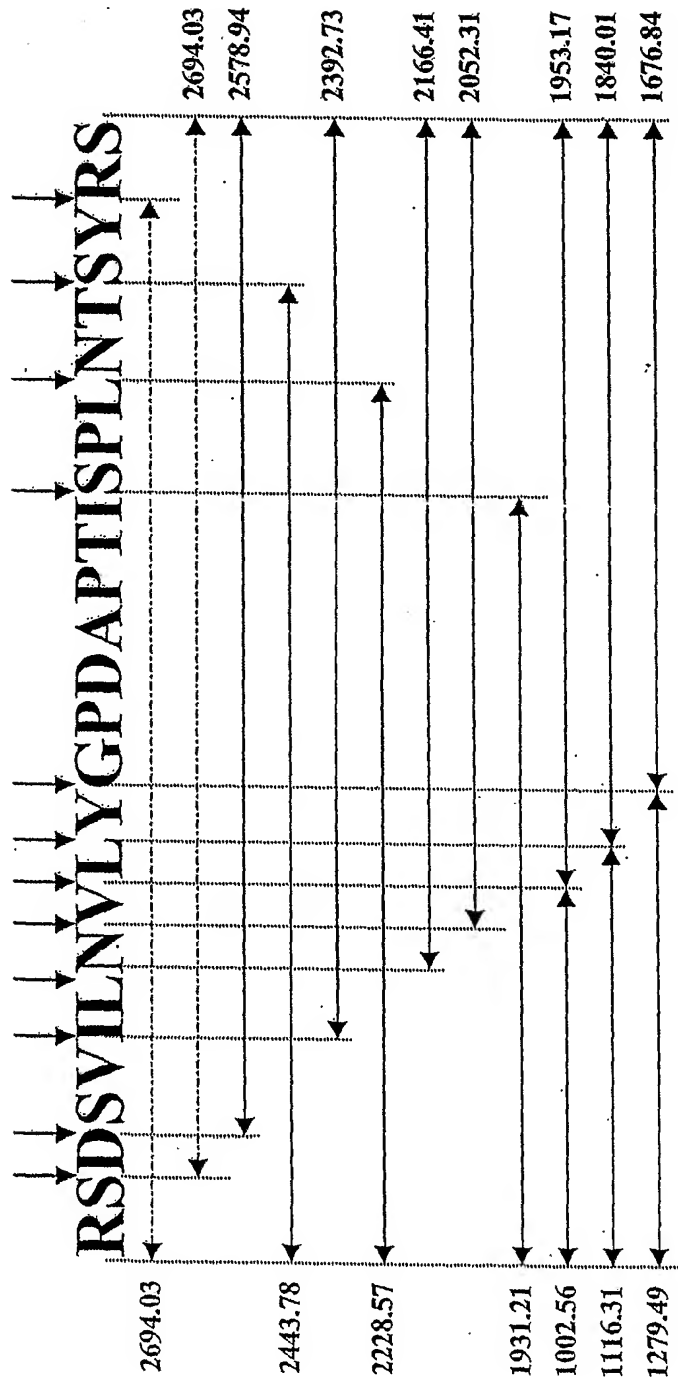


Figure 24

CEA 239-270

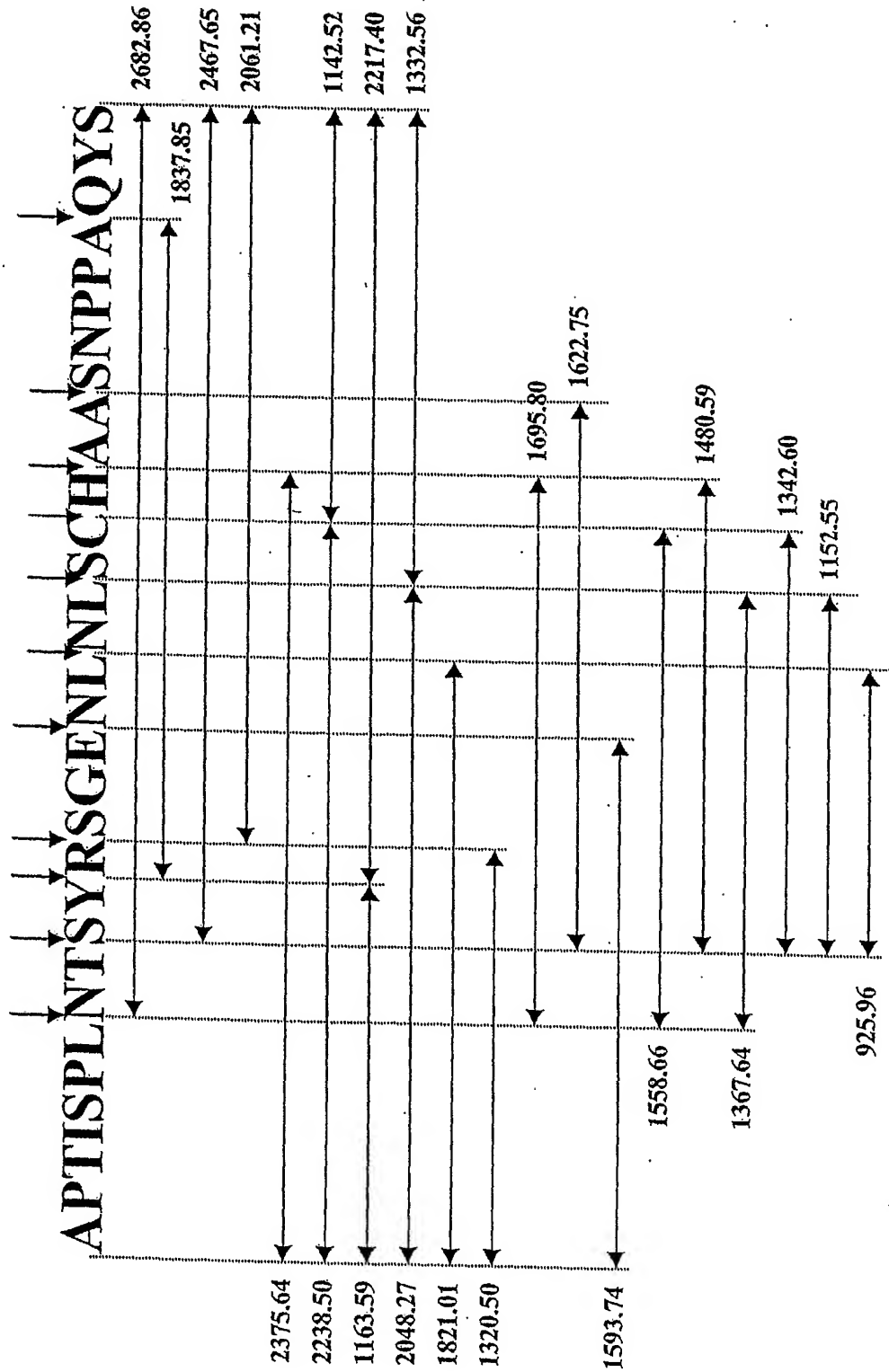


Figure 25

CEA 259-286

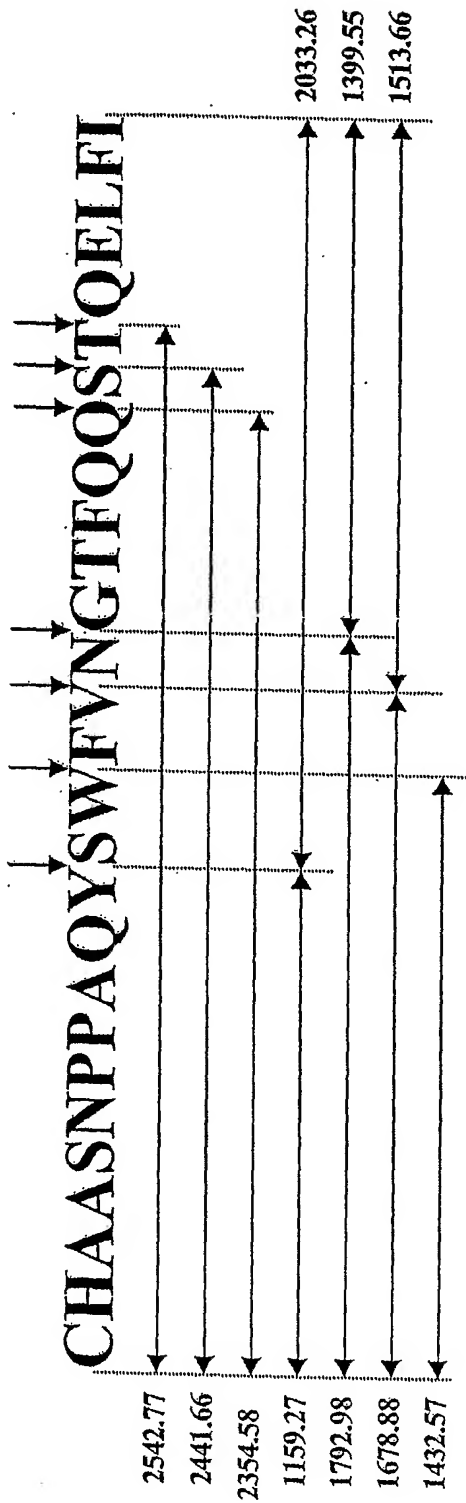


Figure 26

CEA 309-336

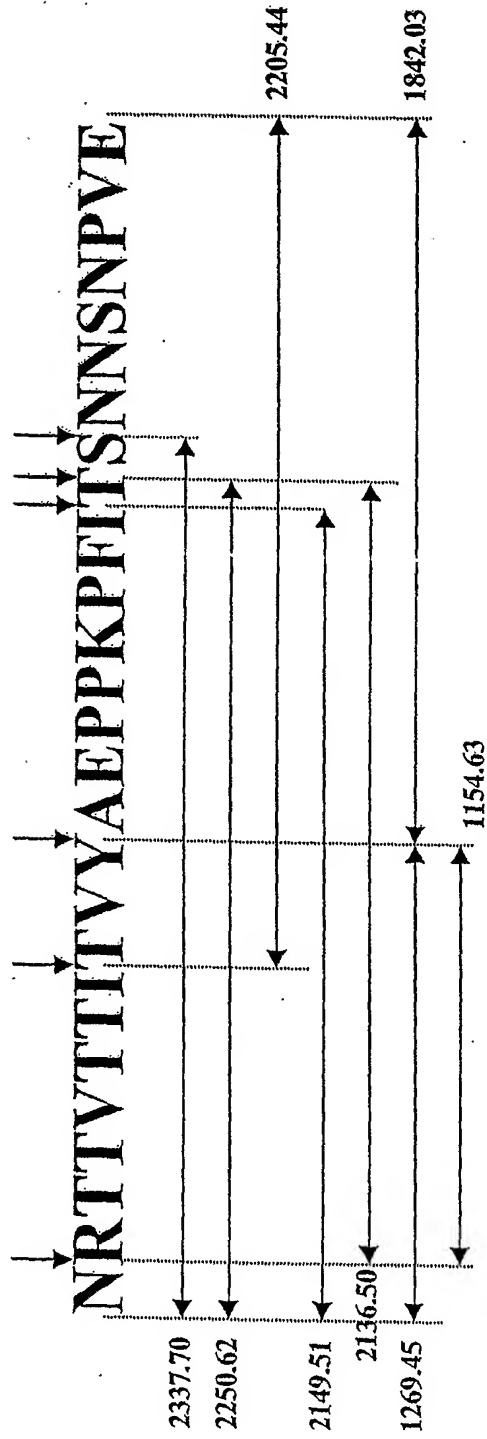


Figure 27

CEA 381-408

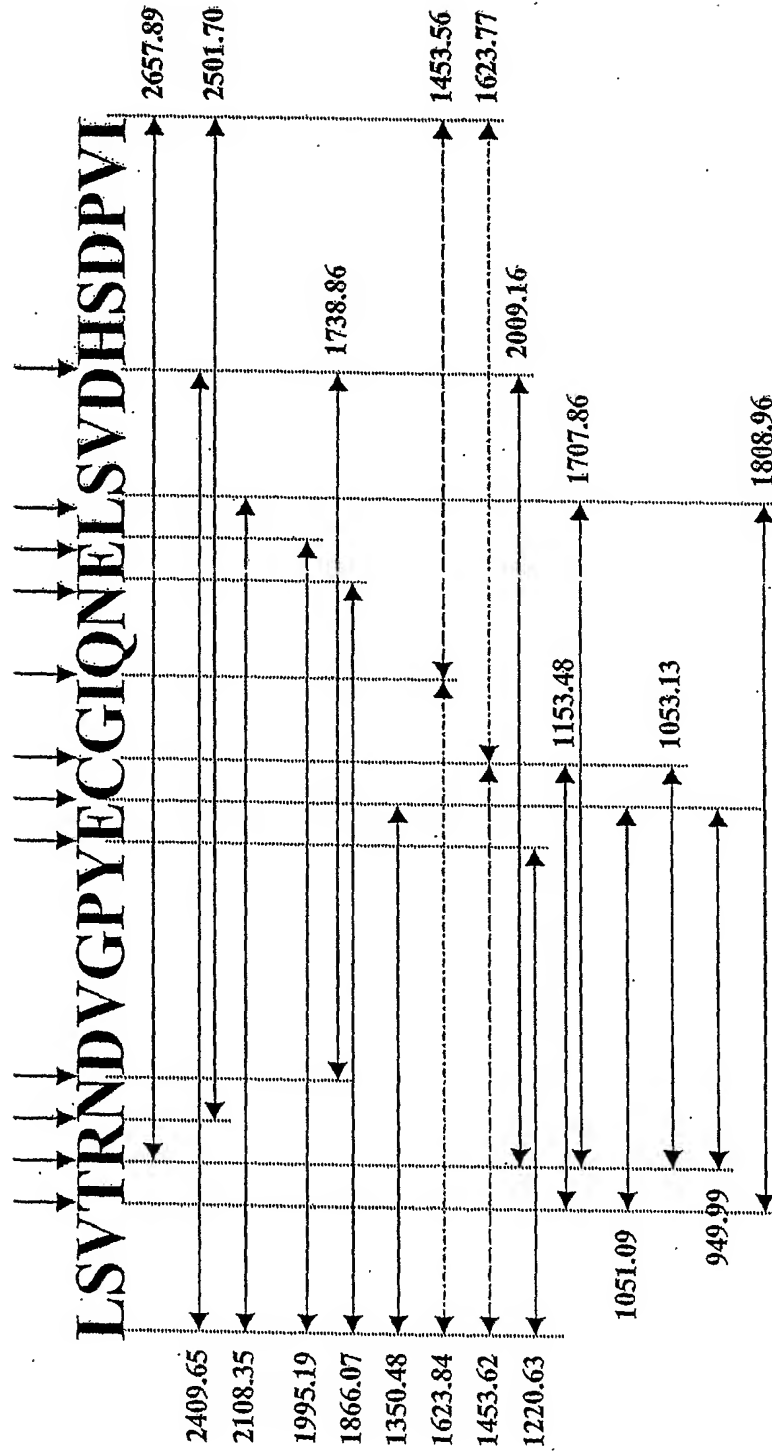


Figure 28

CEA 403-429

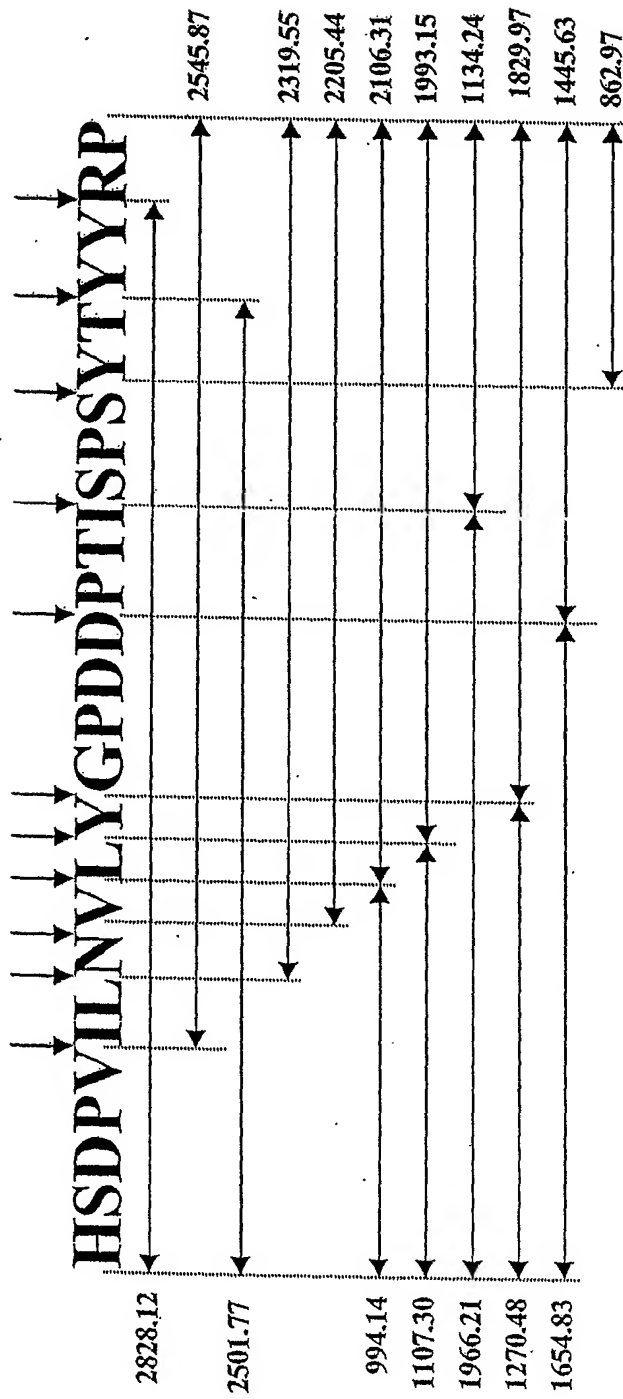


Figure 29

CEA 416-448

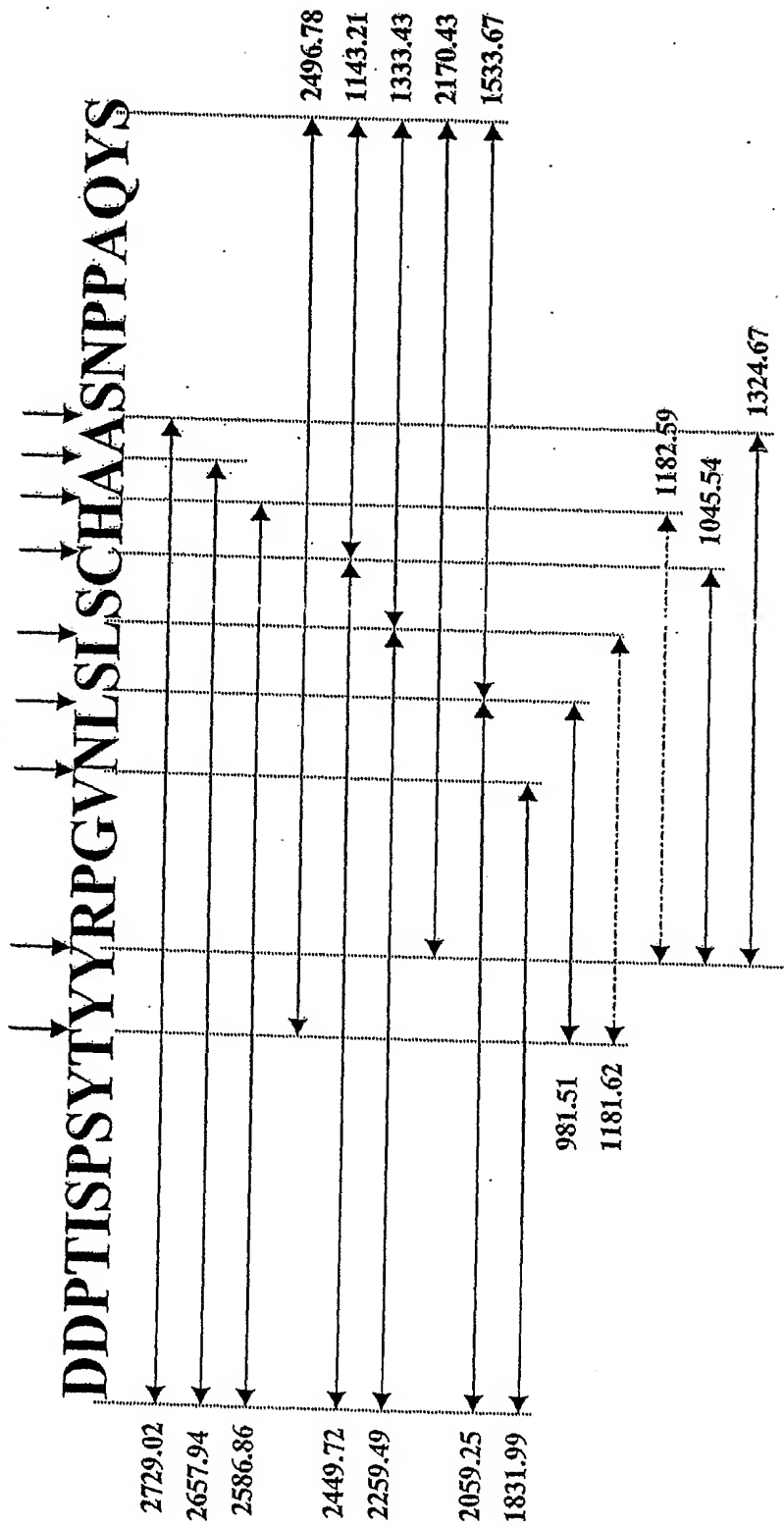


Figure 30

CEA 437-464

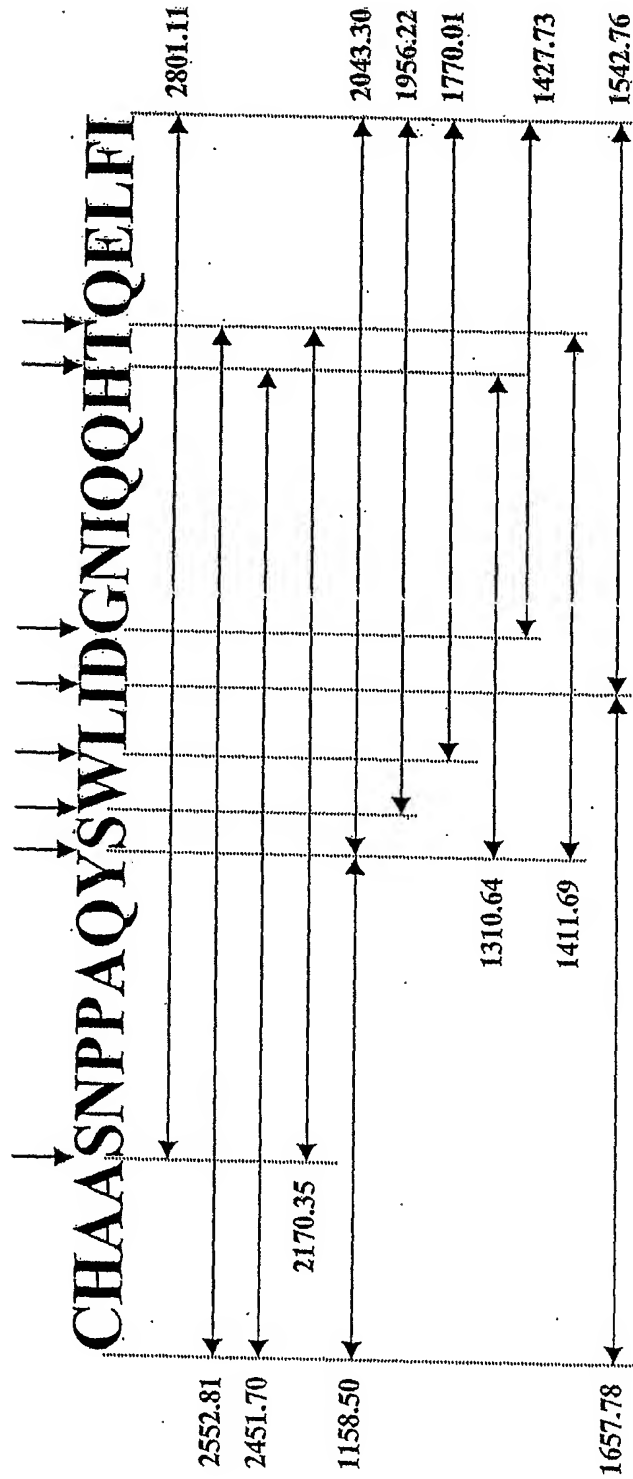


Figure 31

CEA 581-607

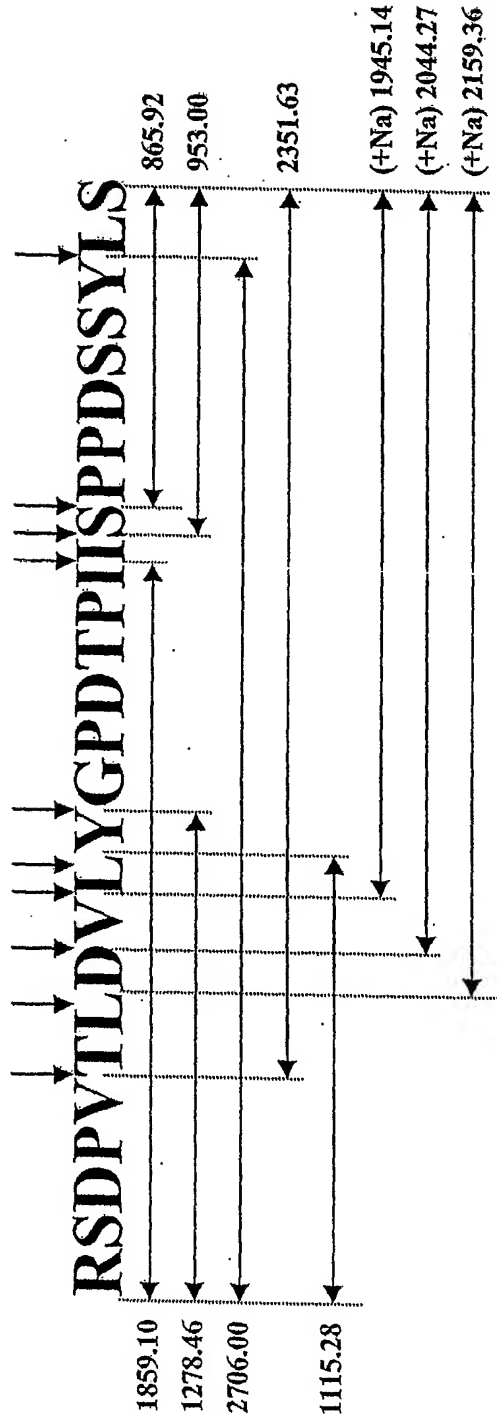


Figure 32

CEA 595-622

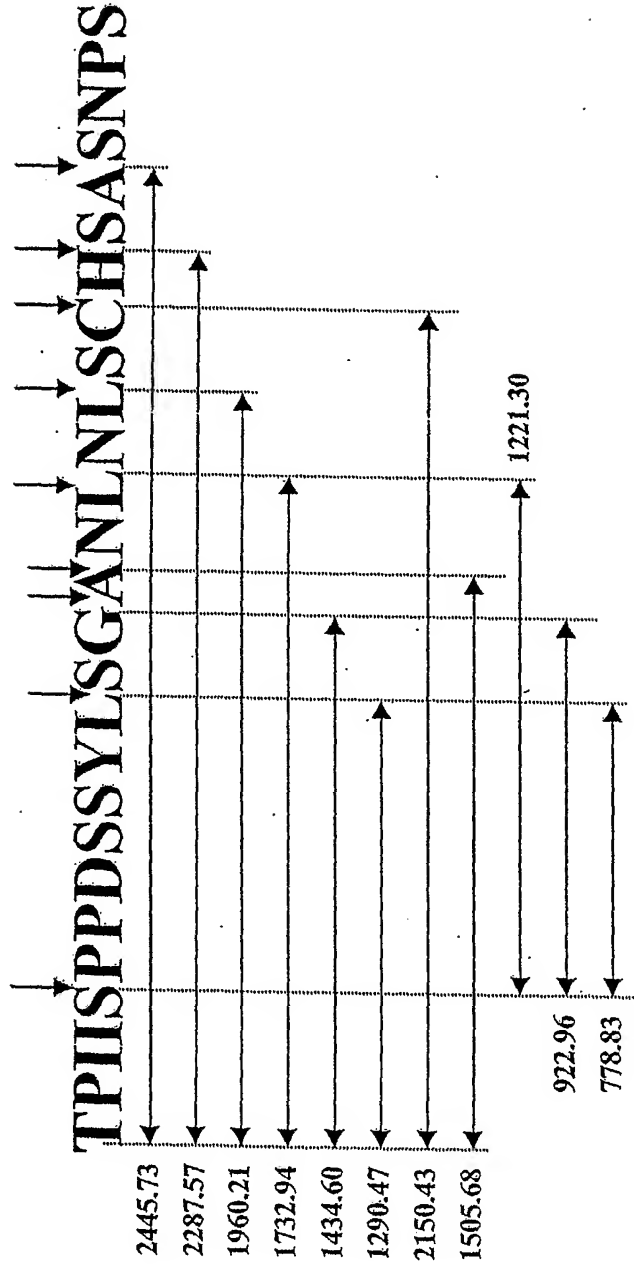


Figure 33

CEA 615-64I

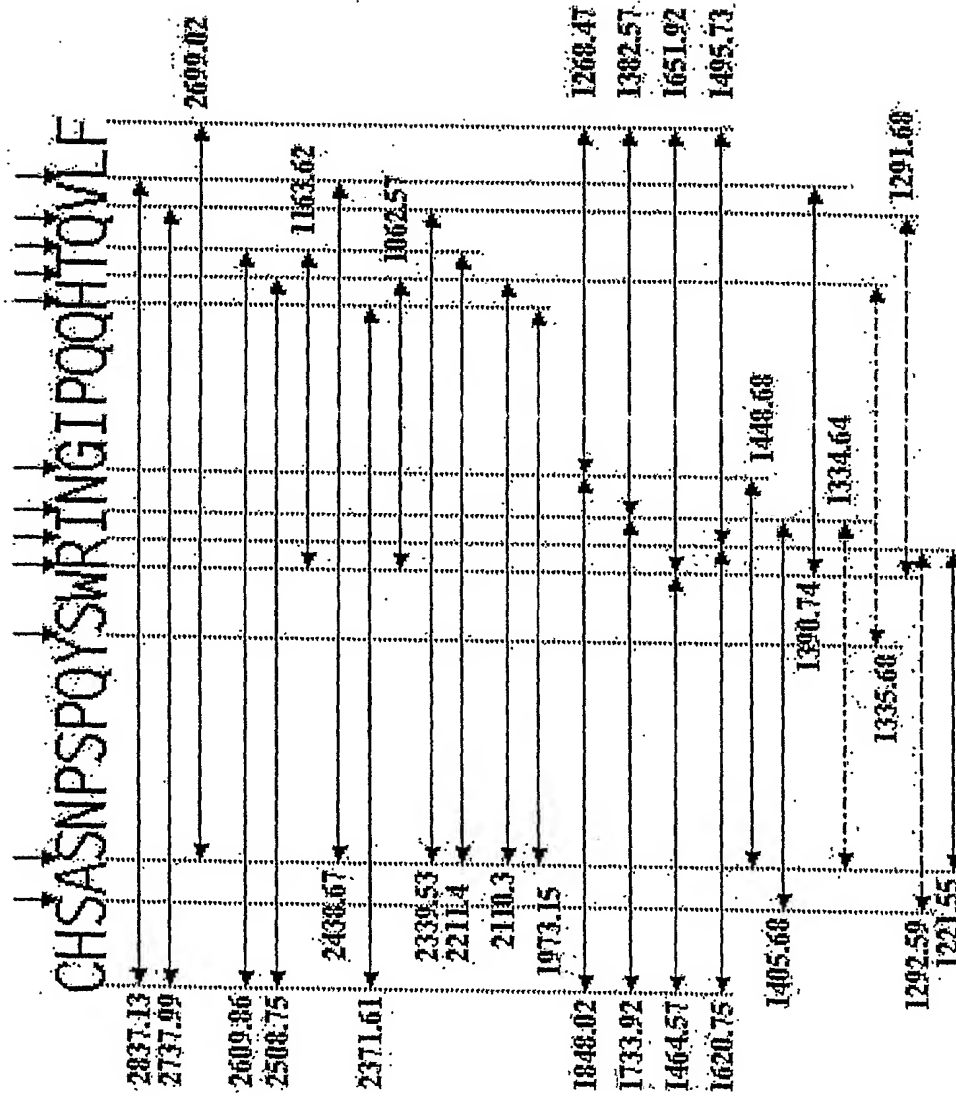


Figure 34

CEA 643-677

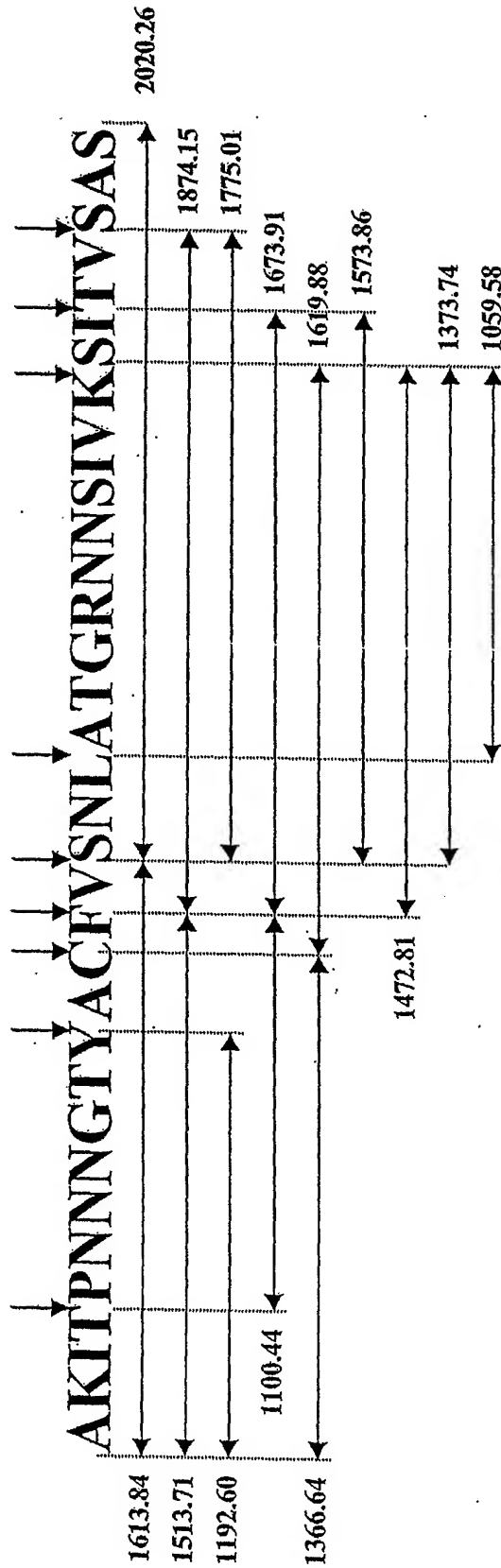


Figure 35

GAGE-1 (6-32) 30 min

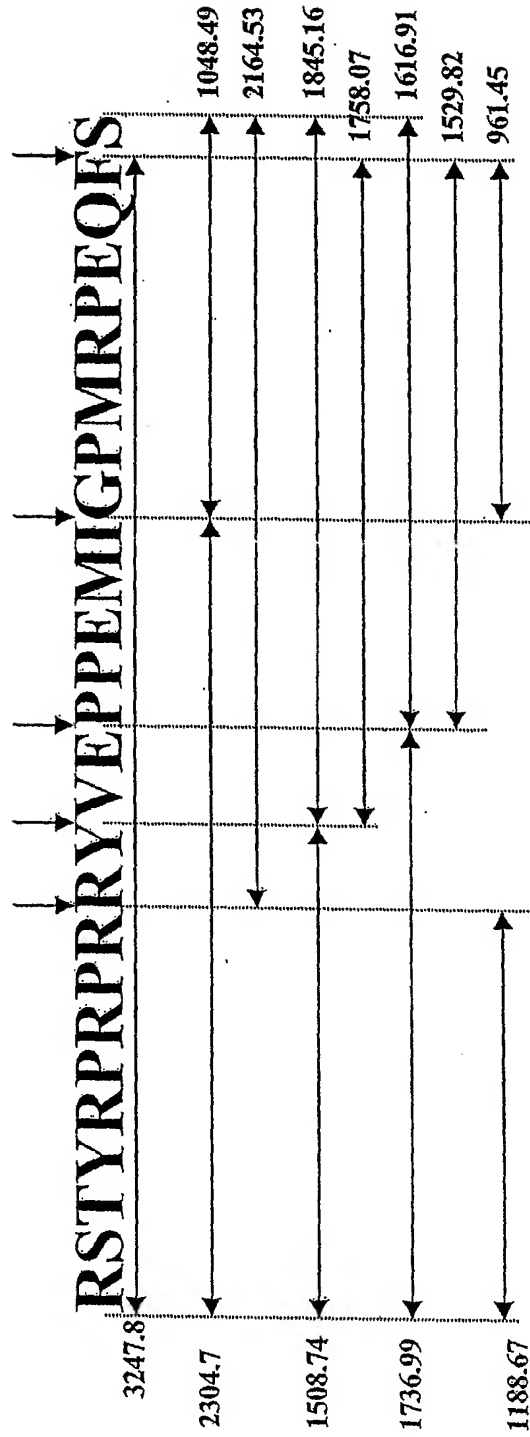


Figure 36

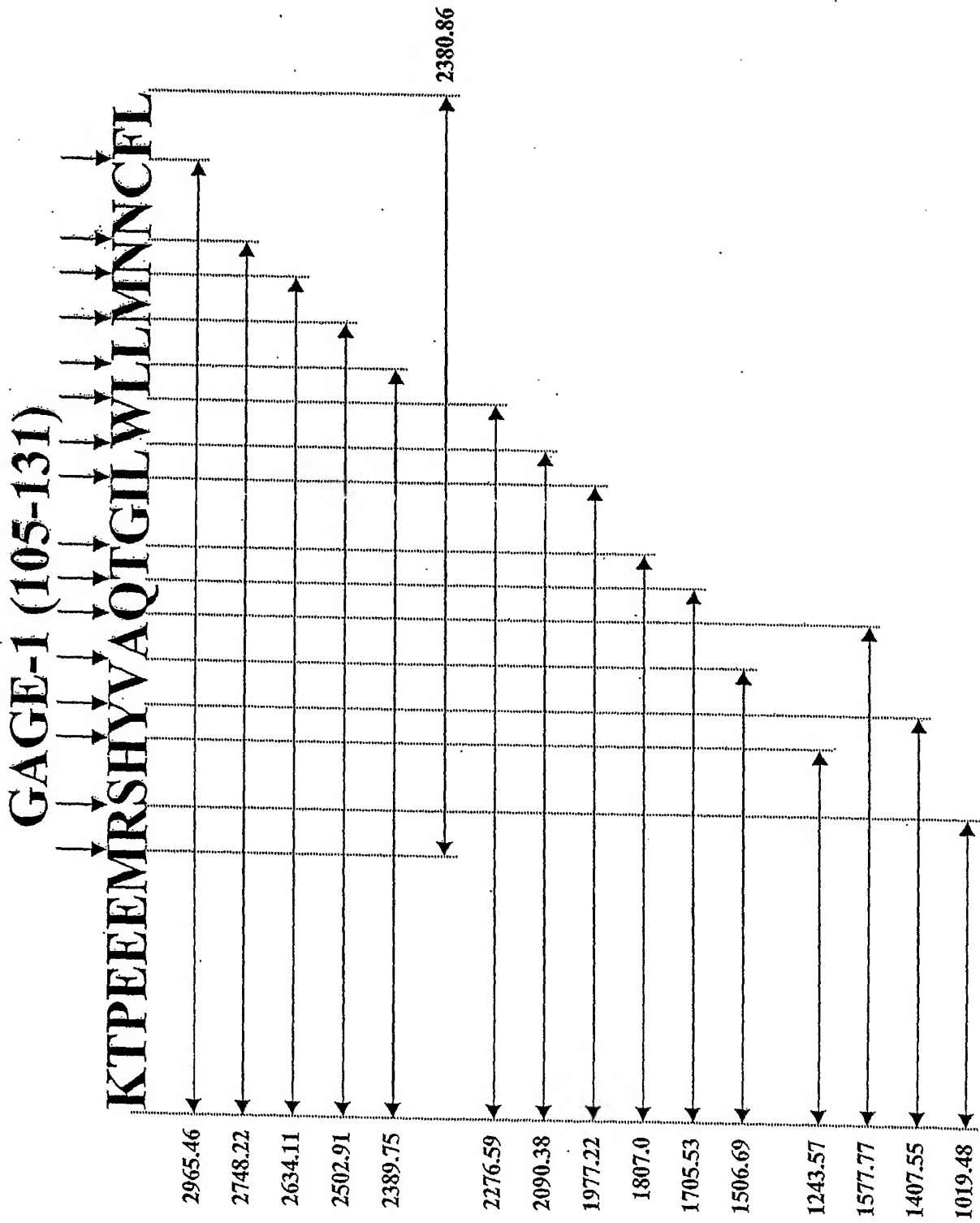


Figure 37

GAGE-1 (112-137)

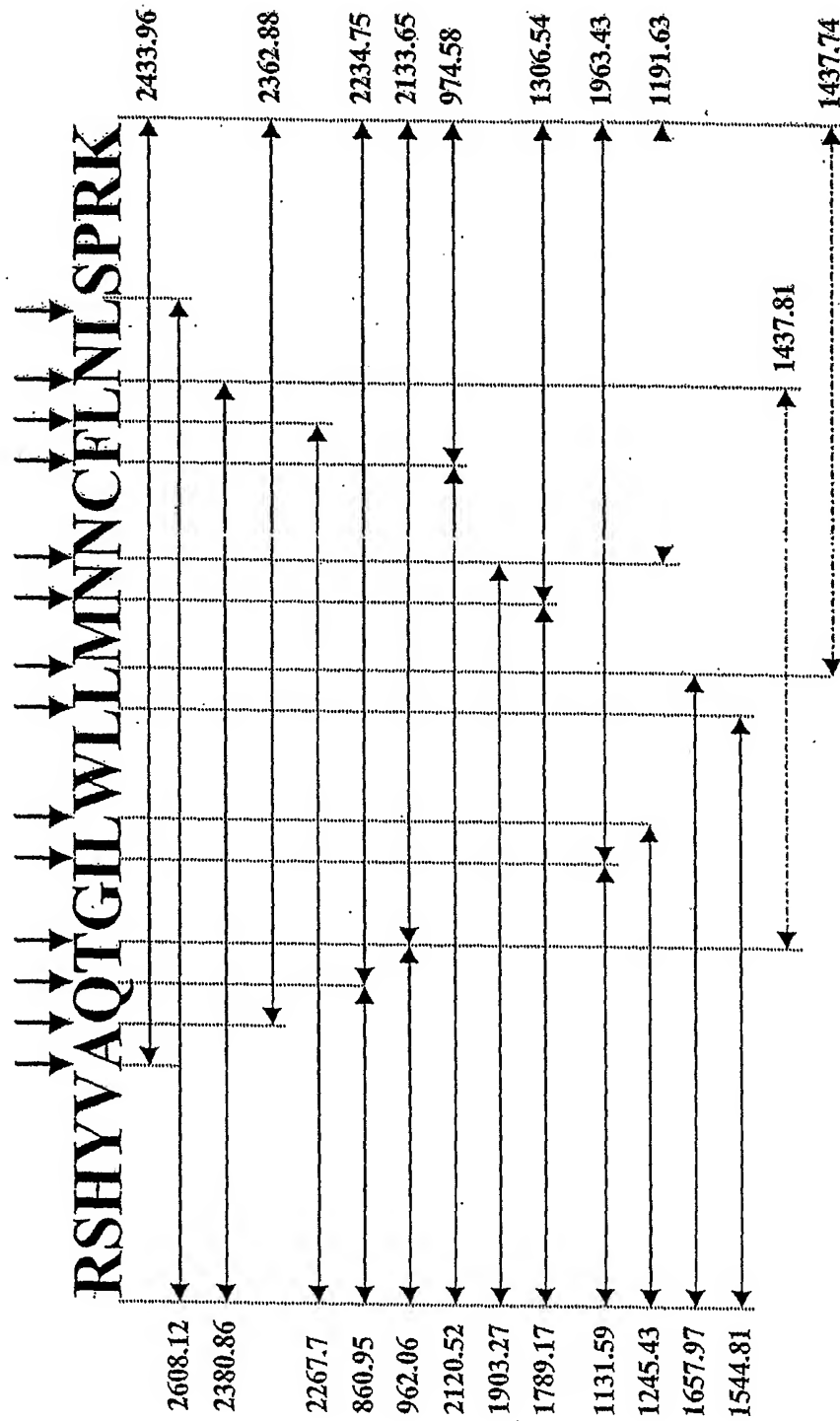


Figure 38

MAGE-1 (51-77)

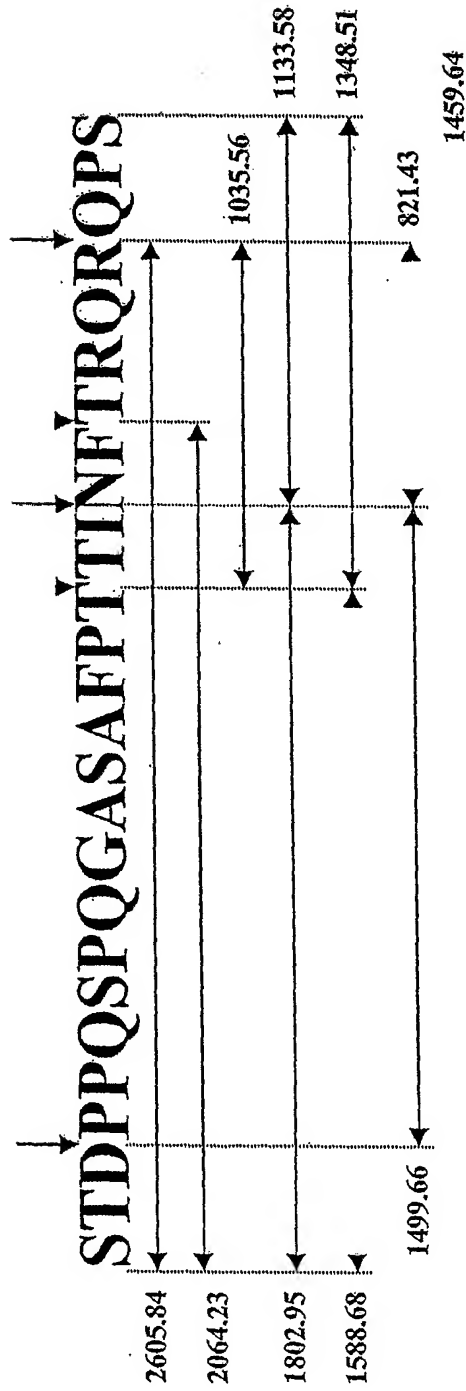


Figure 39

MAGE-1 (126-153)

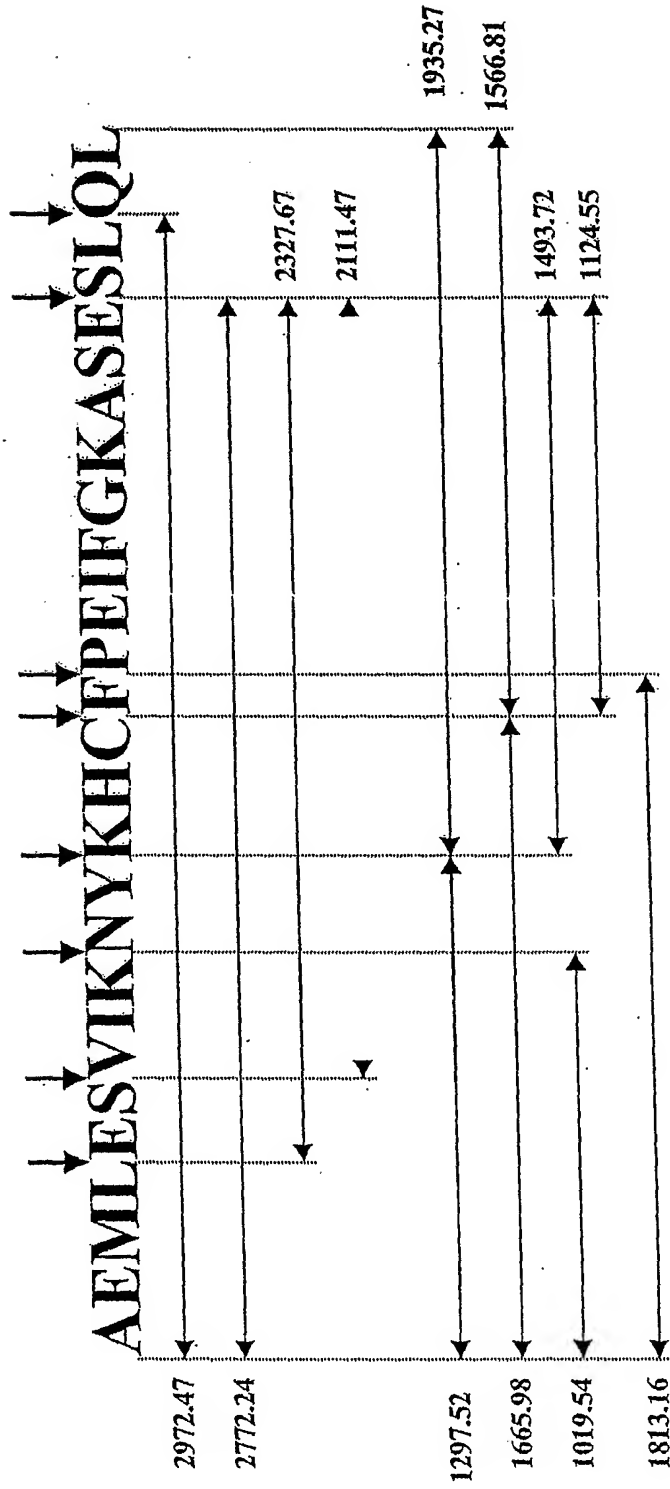
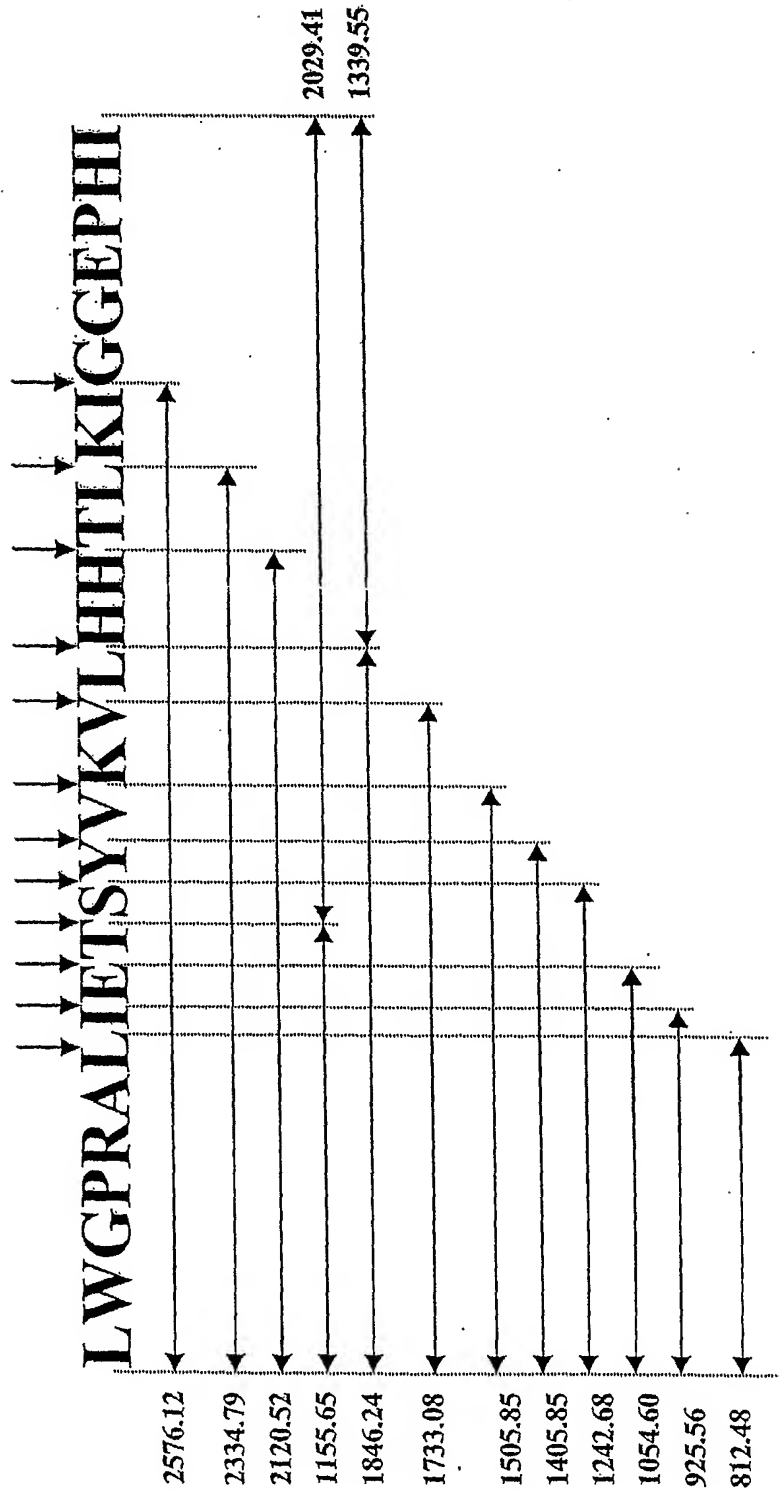


Figure 40

MAGE-2 (272-299)**Figure 41**

MAGE-2 (287-314)

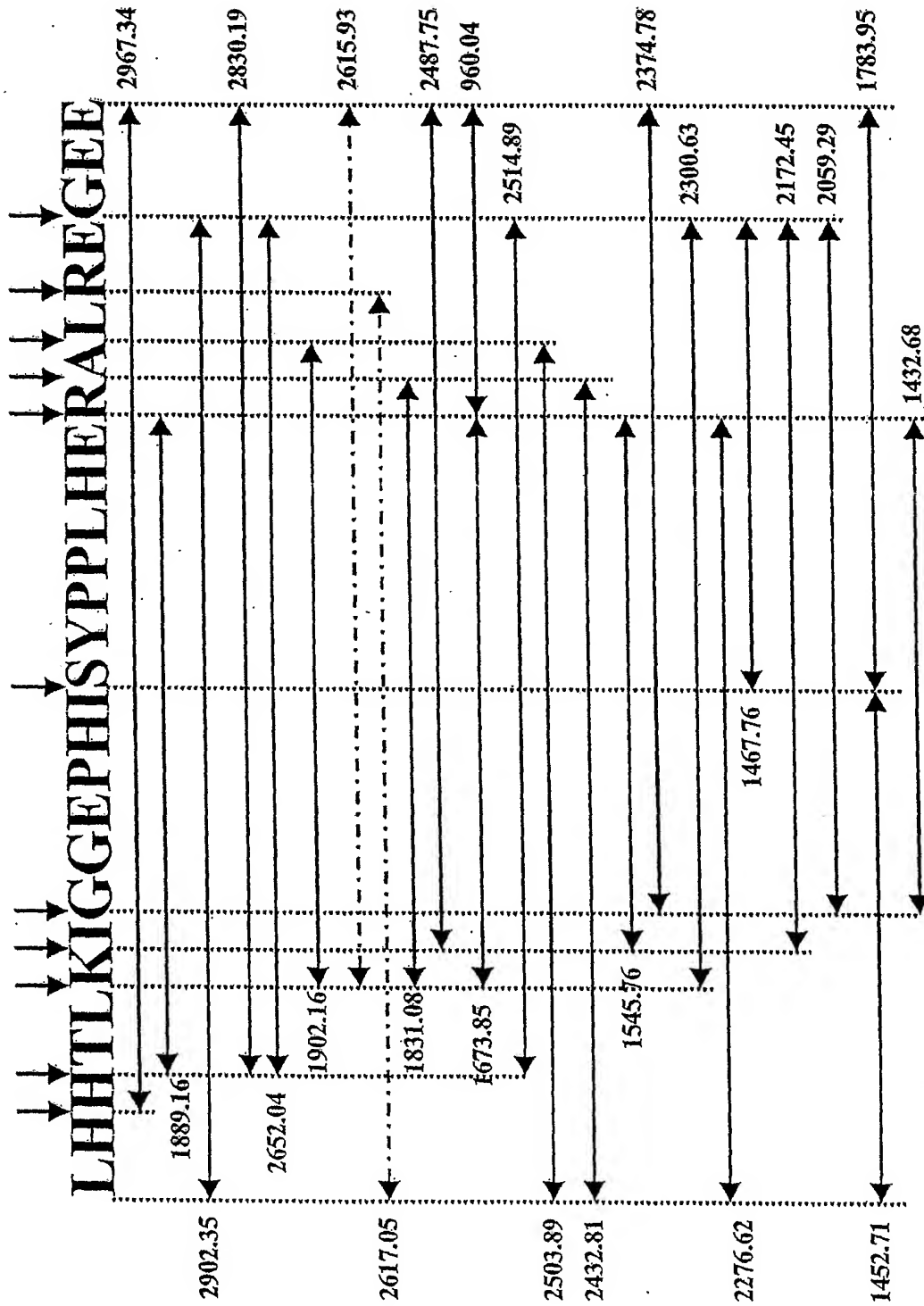


Figure 42

MAGE-3 (287-314)

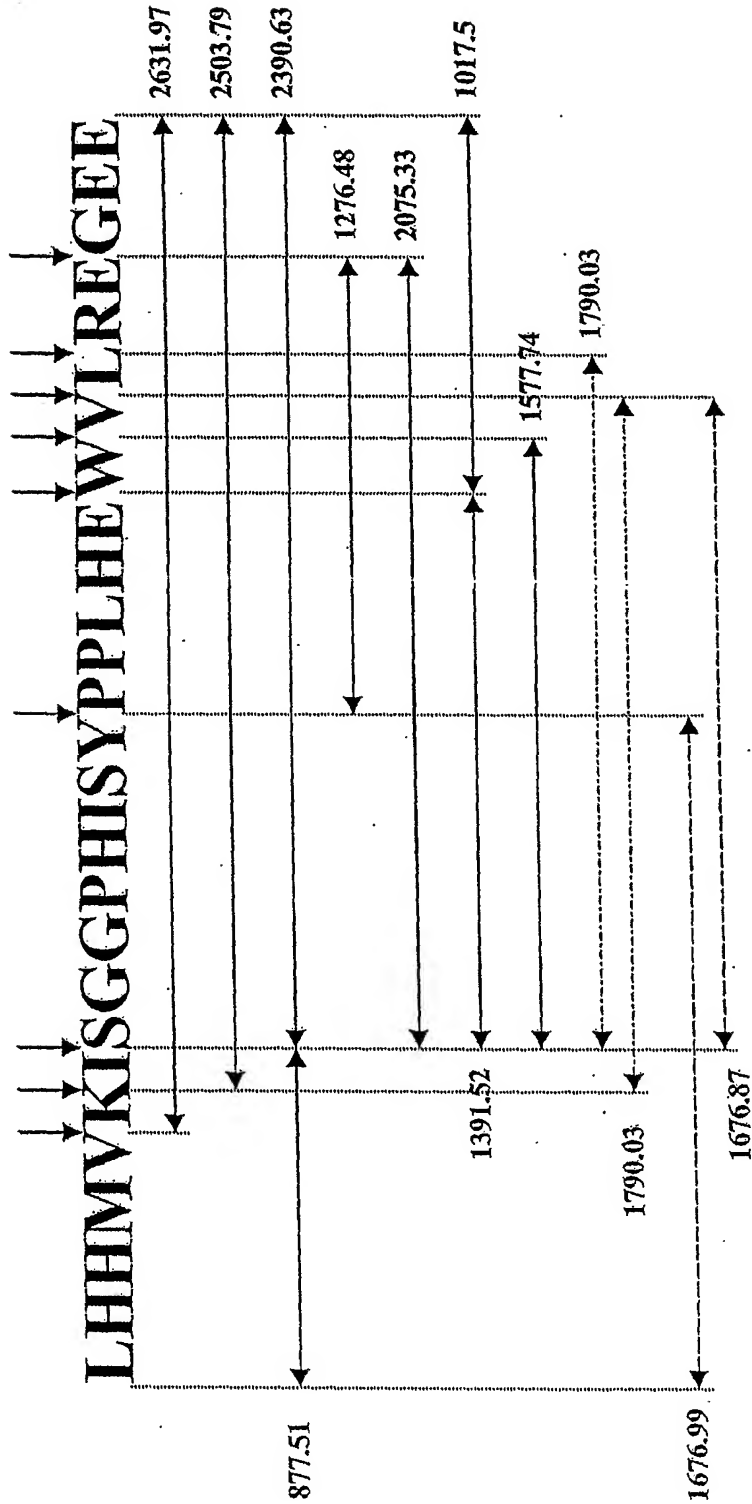


Figure 43

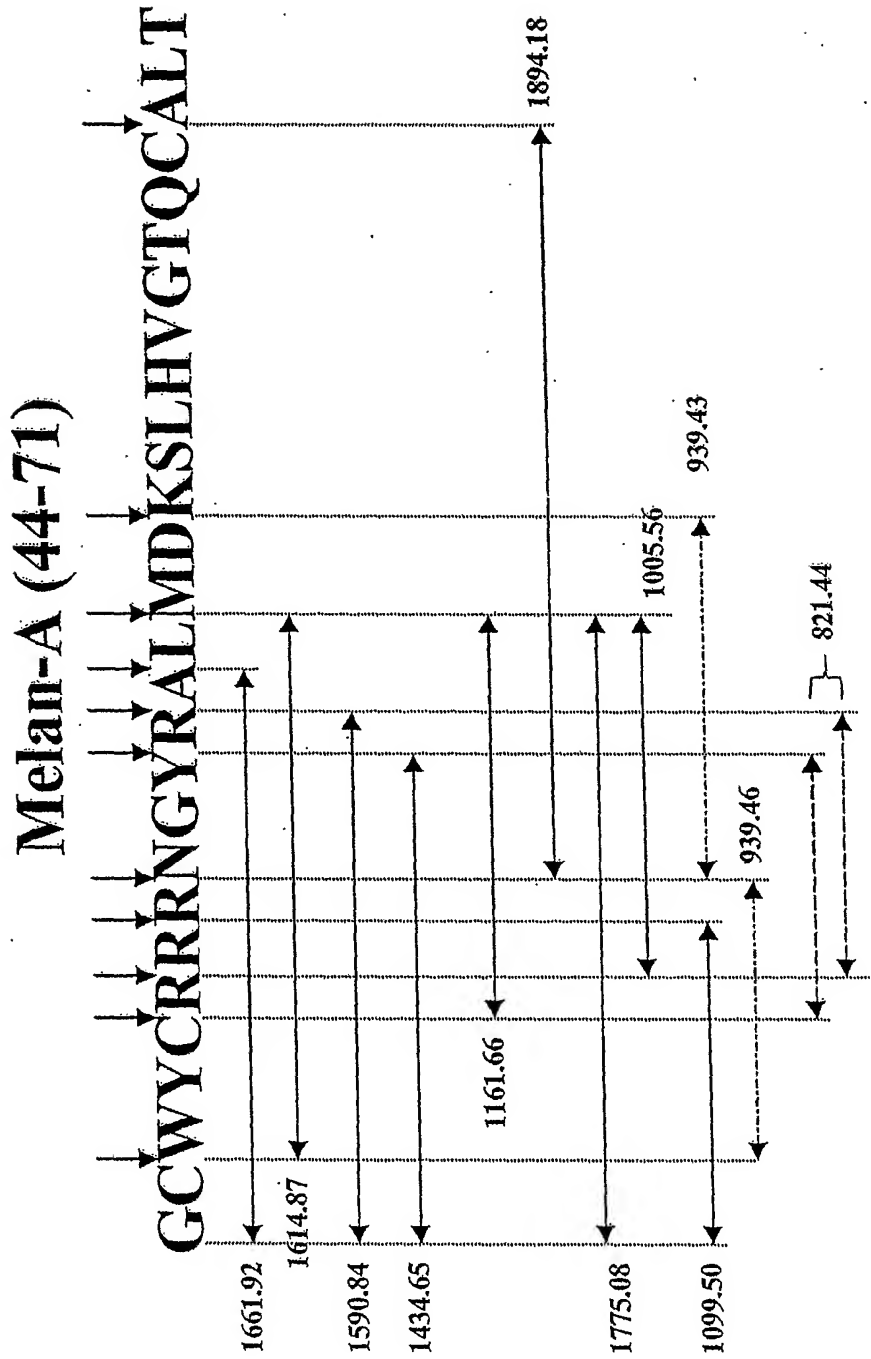


Figure 44

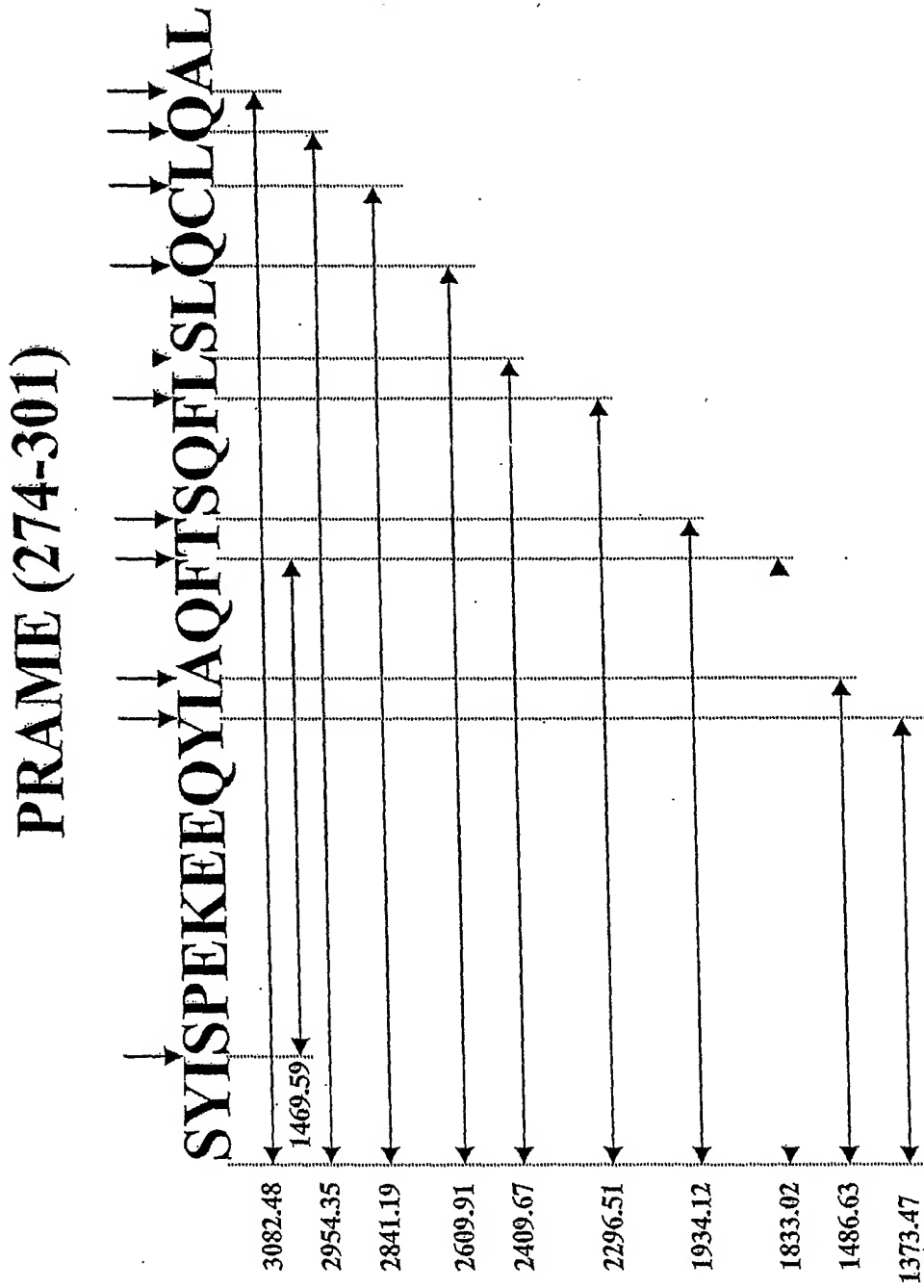


Figure 45

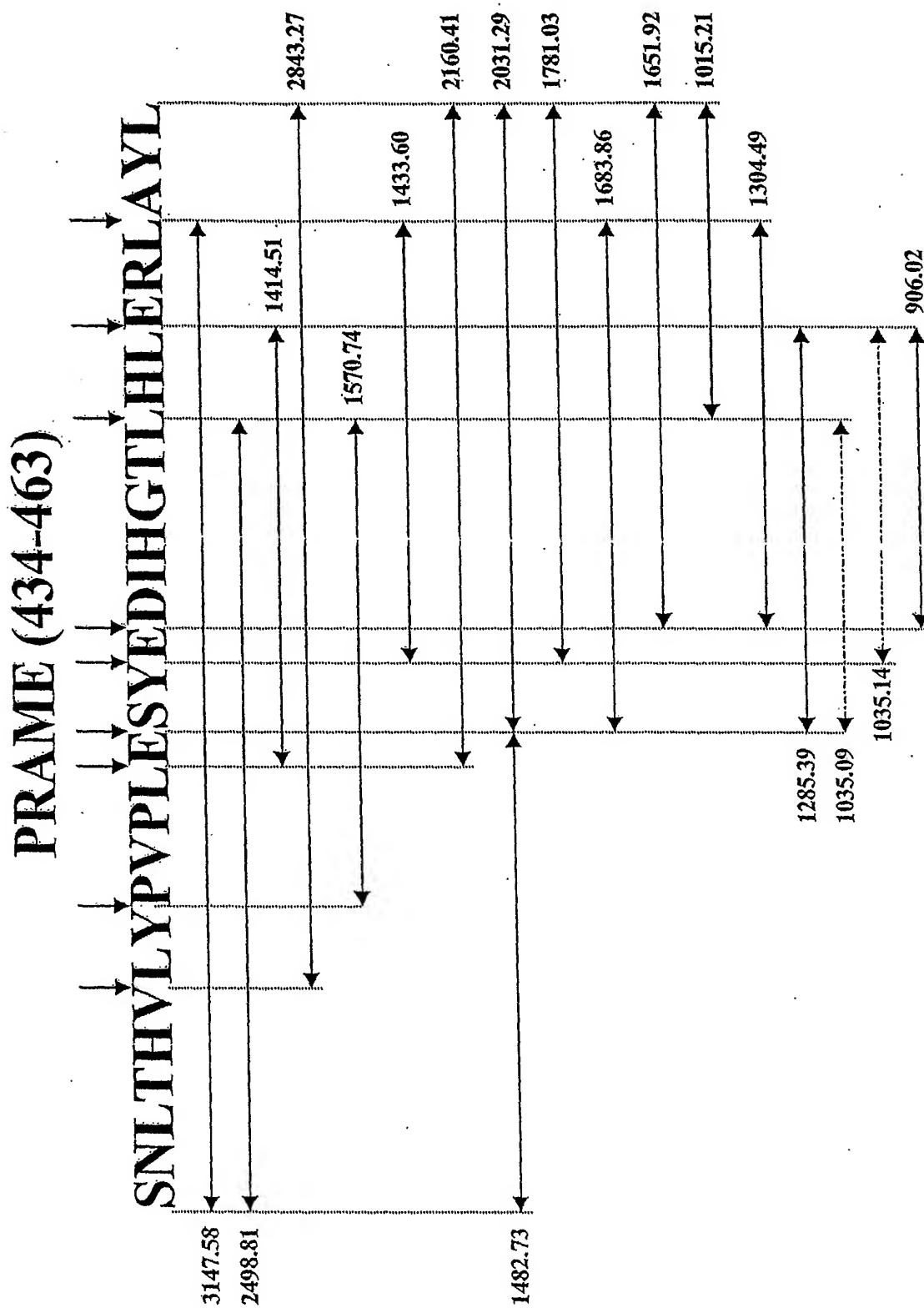


Figure 46

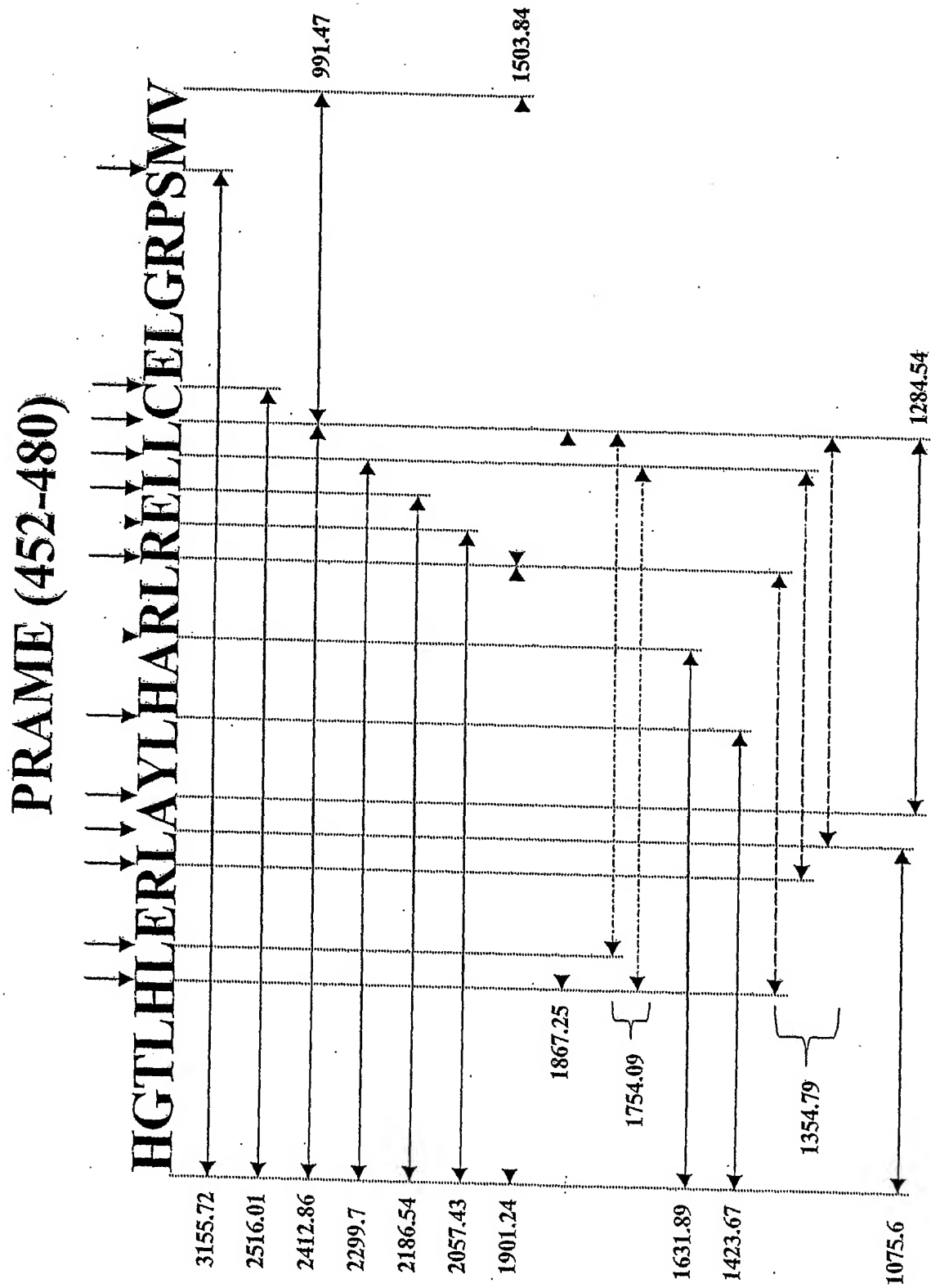


Figure 47

PSA (143-169)

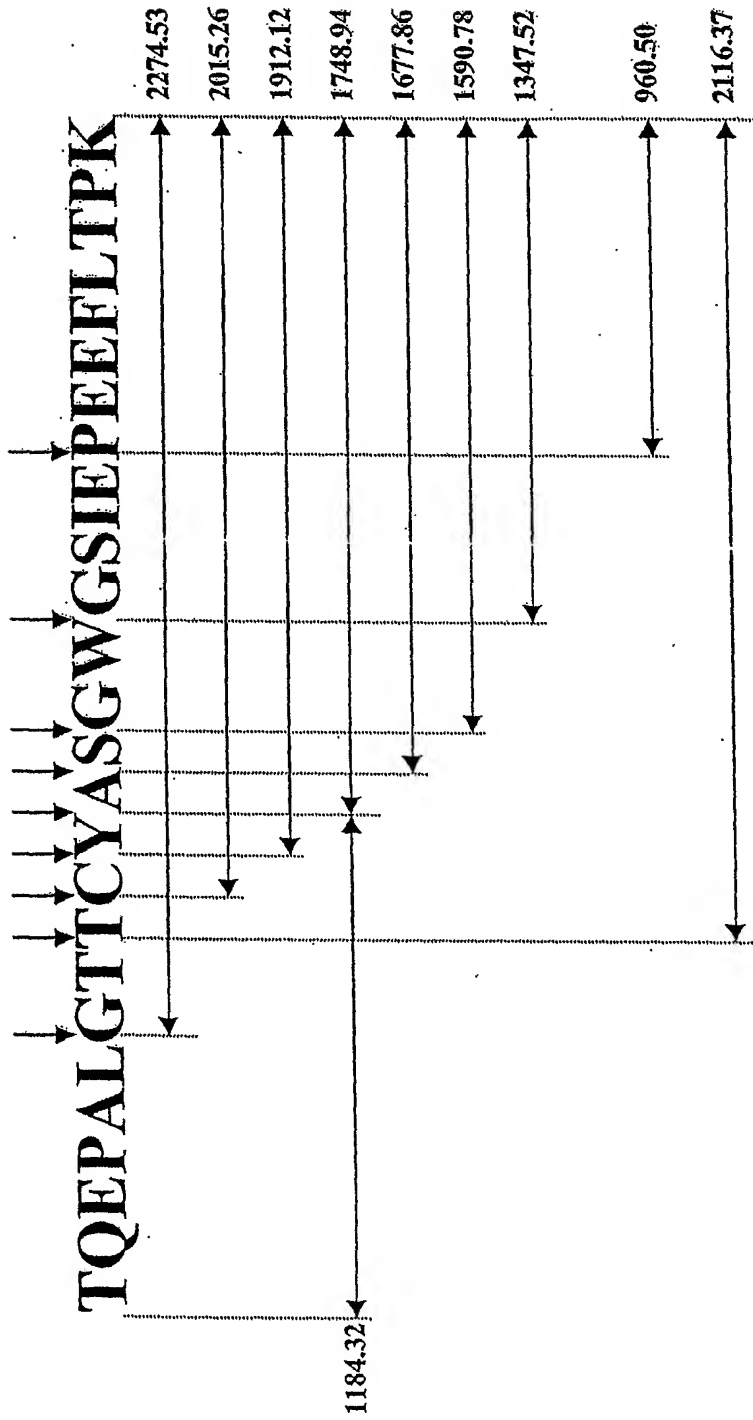


Figure 48

PSA 156-188

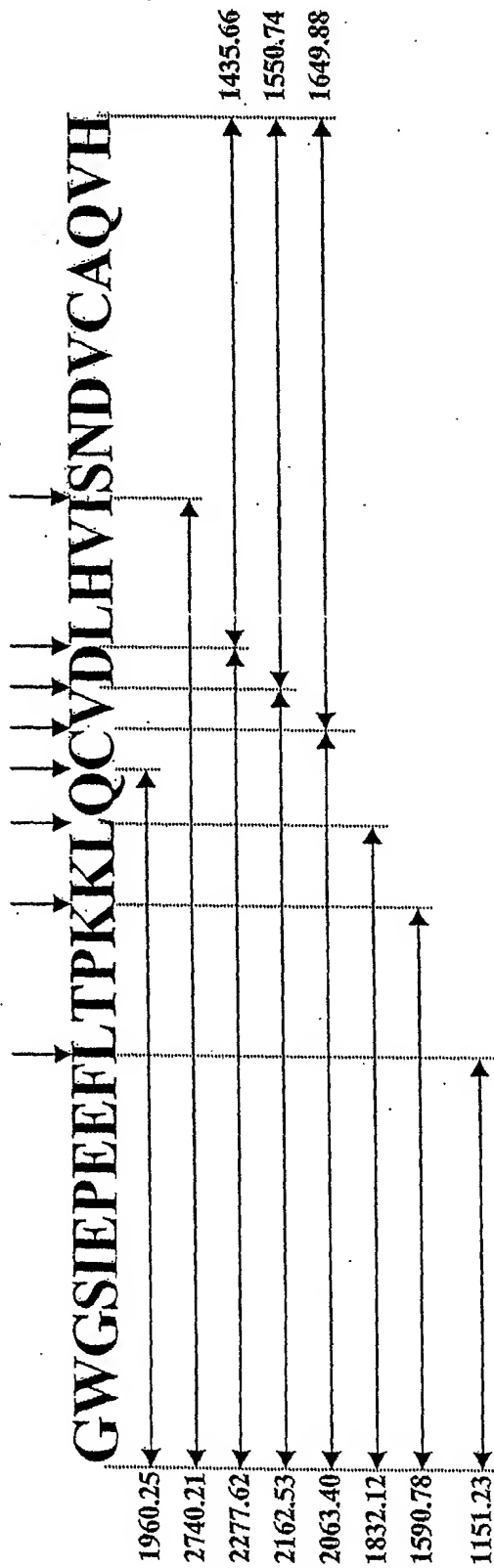


Figure 49

PSCA 67-94

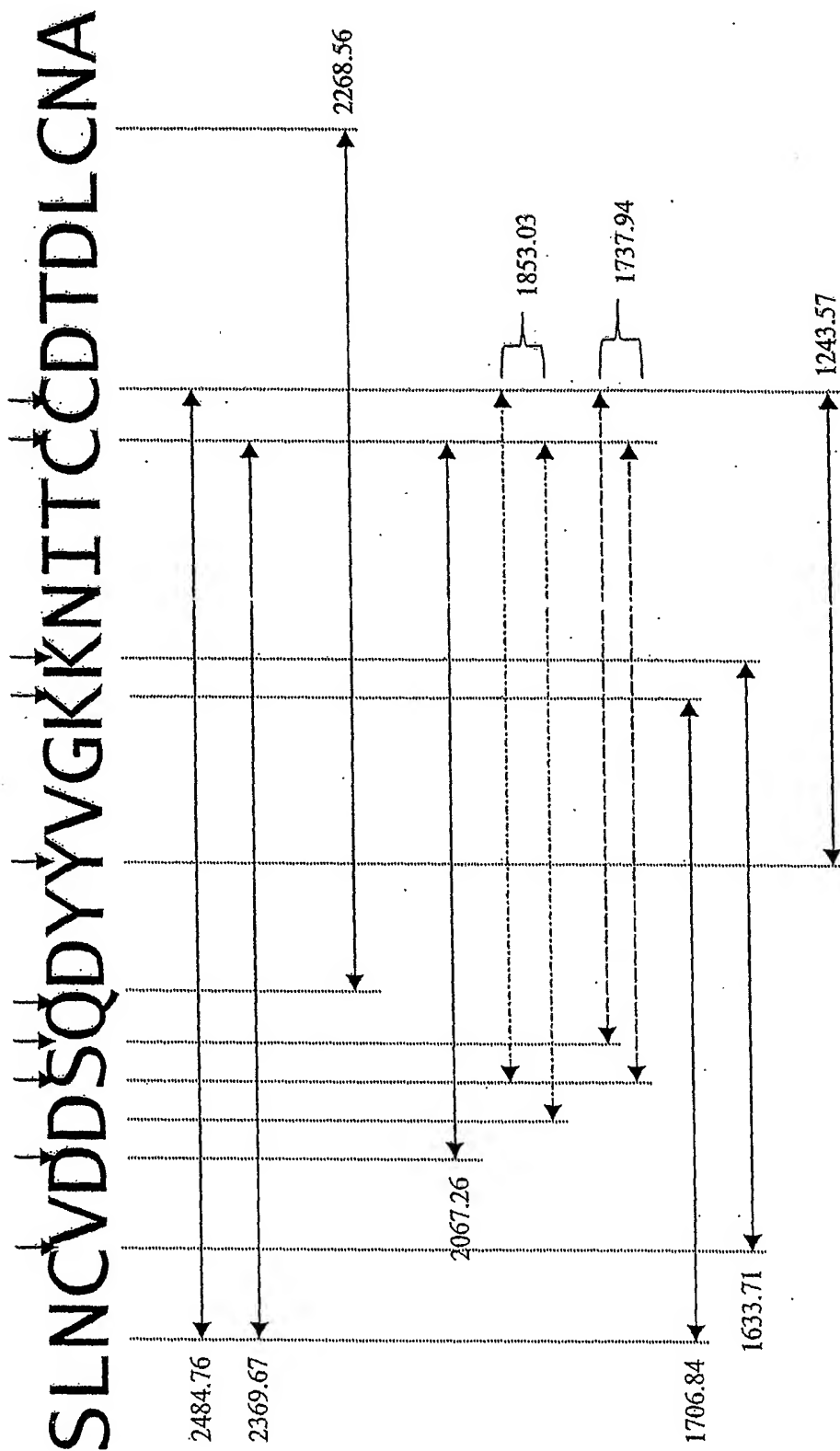


Figure 50

PSMA (378-405)

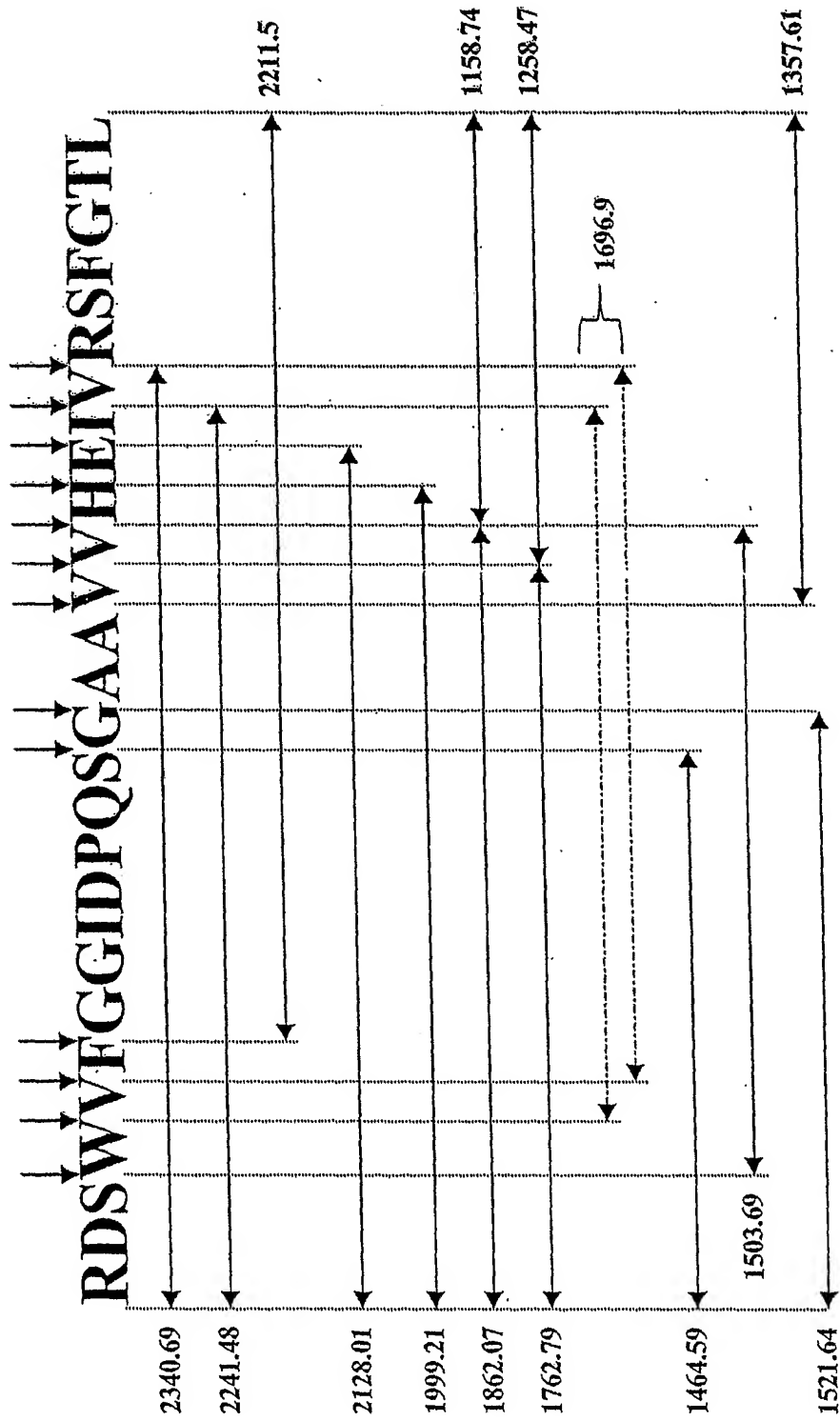


Figure 51

PSMA (597-623)

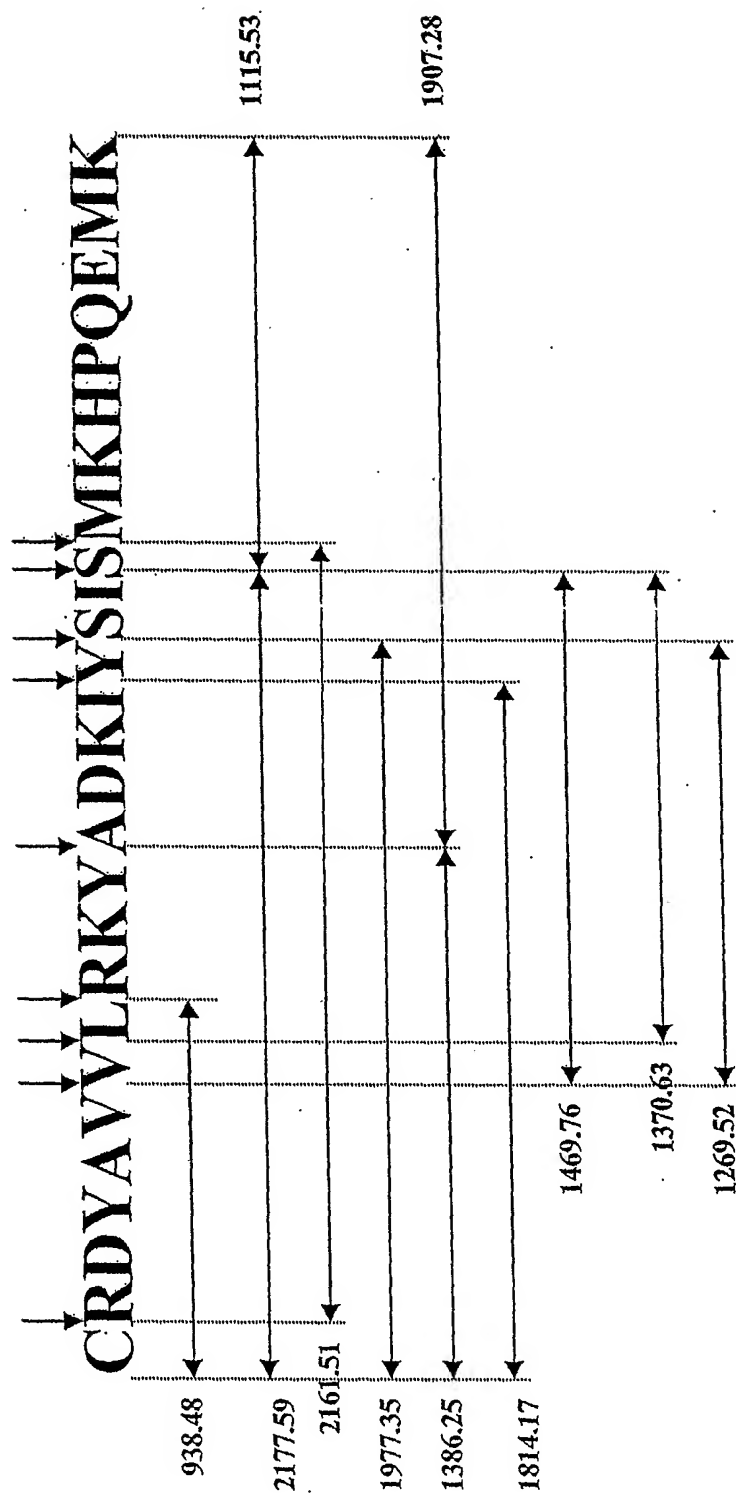


Figure 52

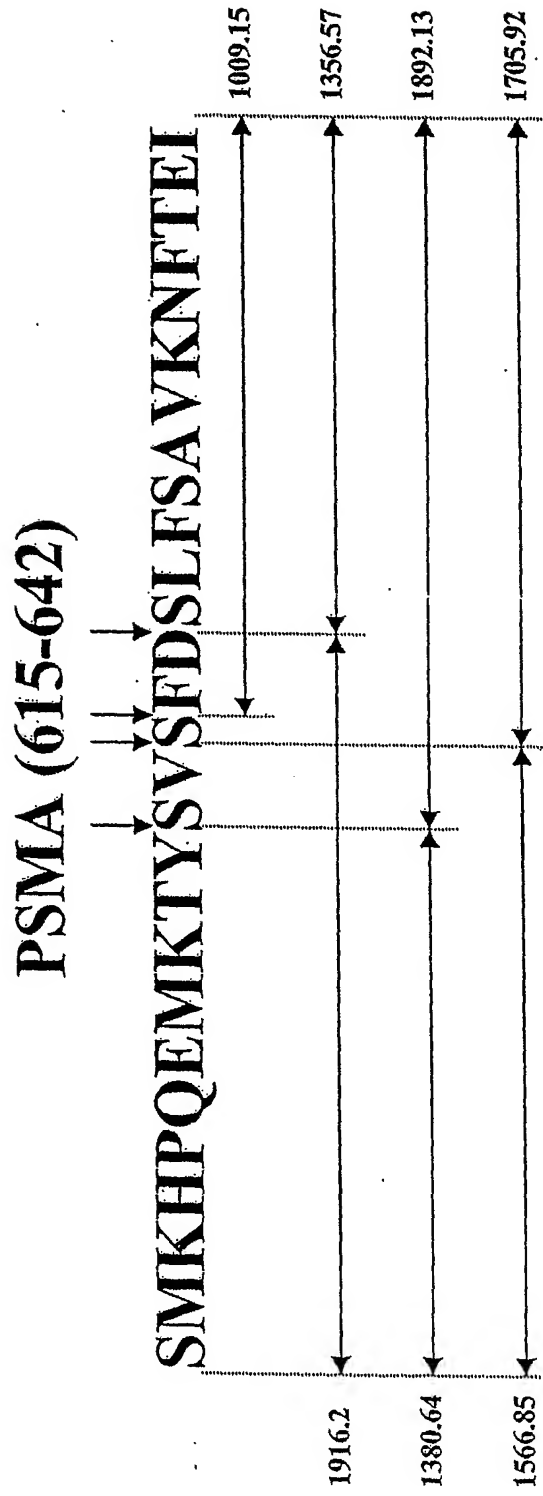


Figure 53

SCP-1 (57-86)

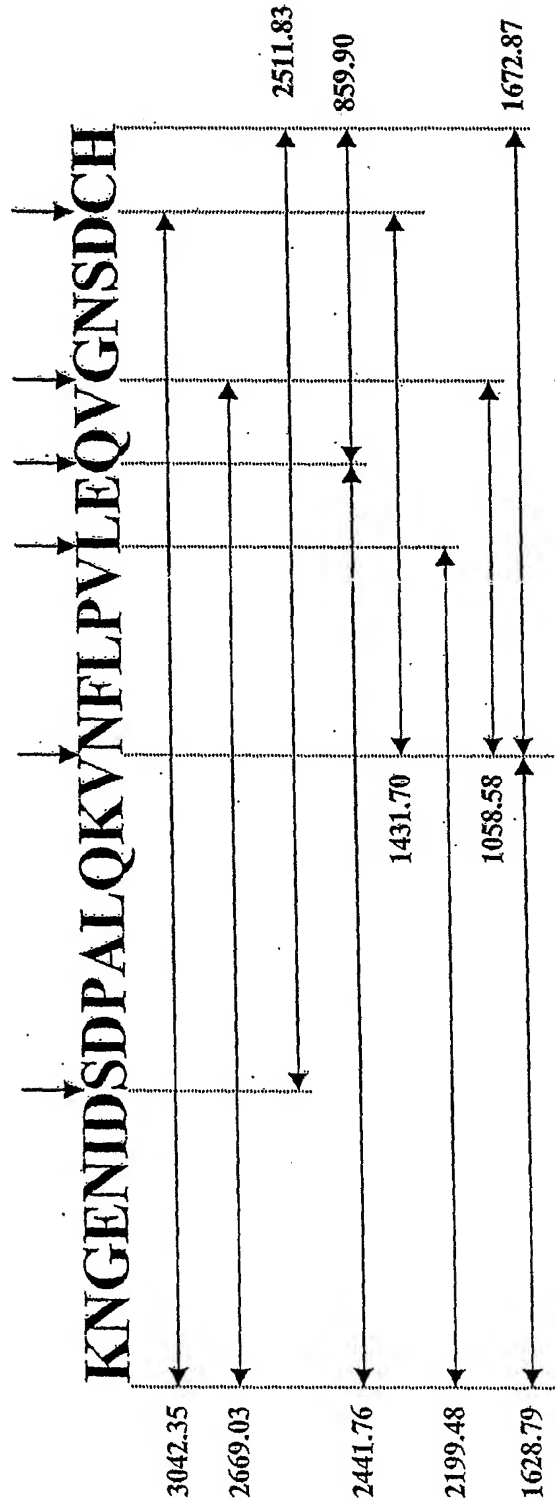


Figure 54

SCP-1 (201-227)

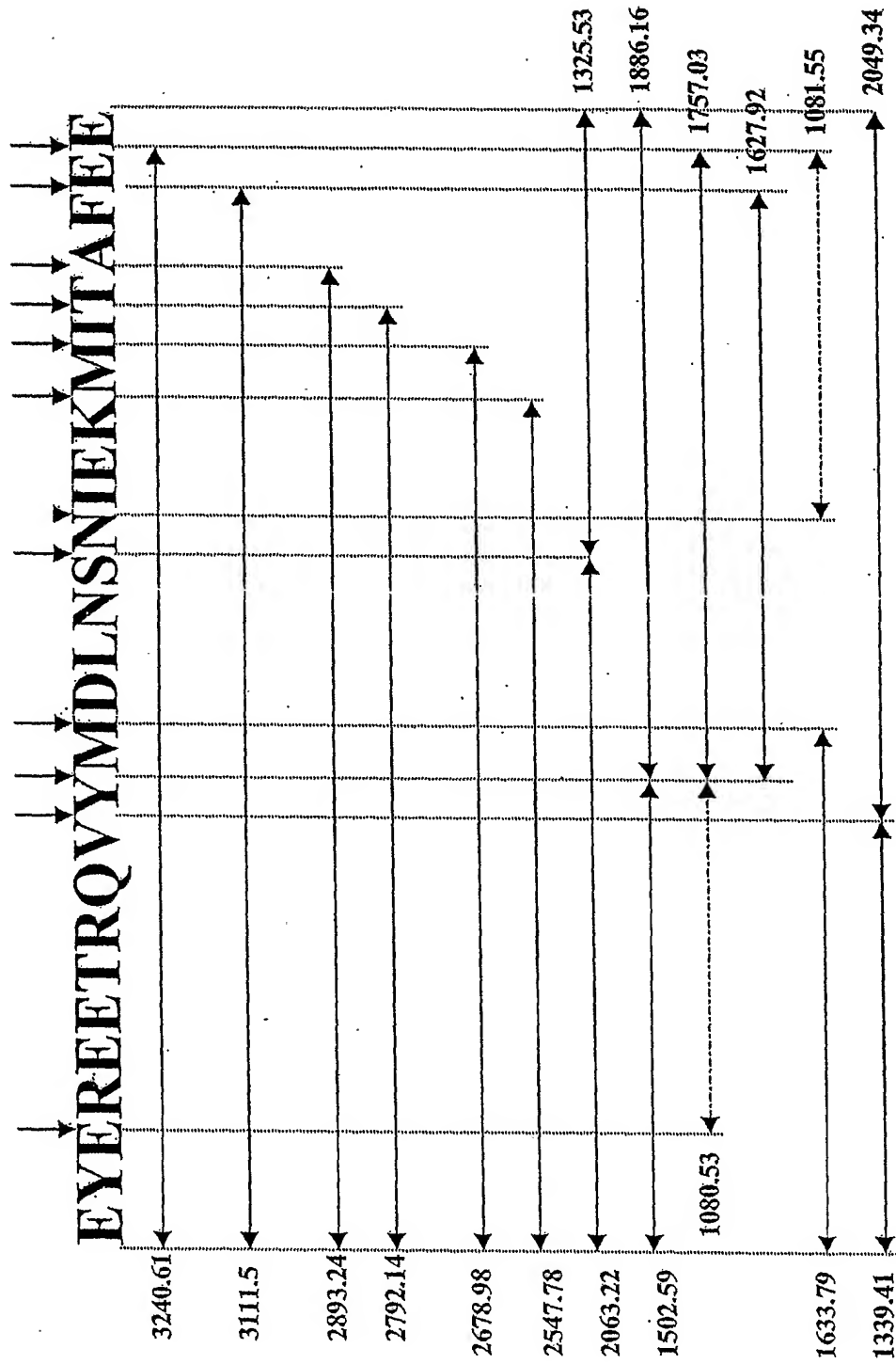


Figure 55

SCP-1 (395-424)

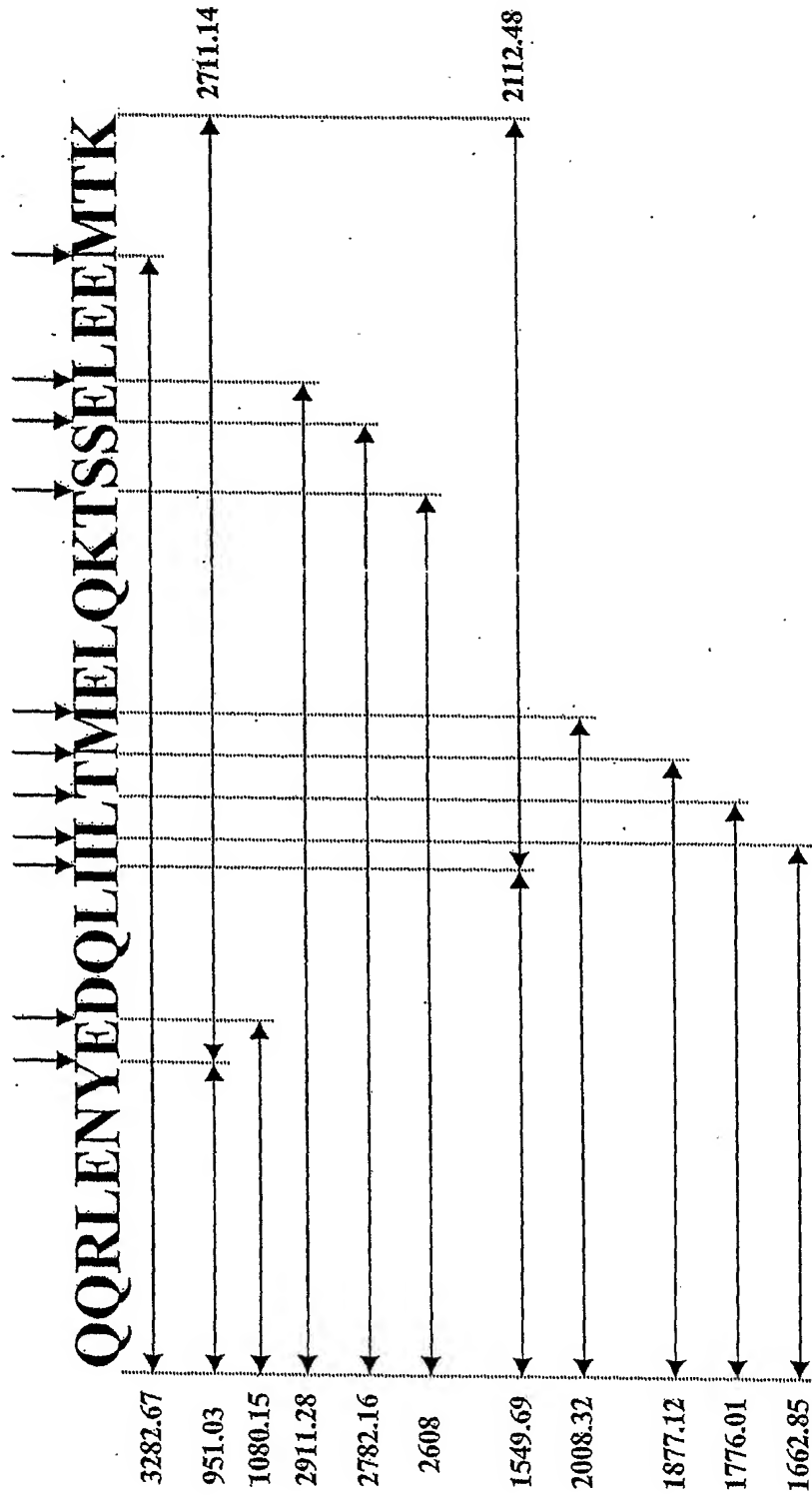


Figure 56

SCP-1 (416-442)

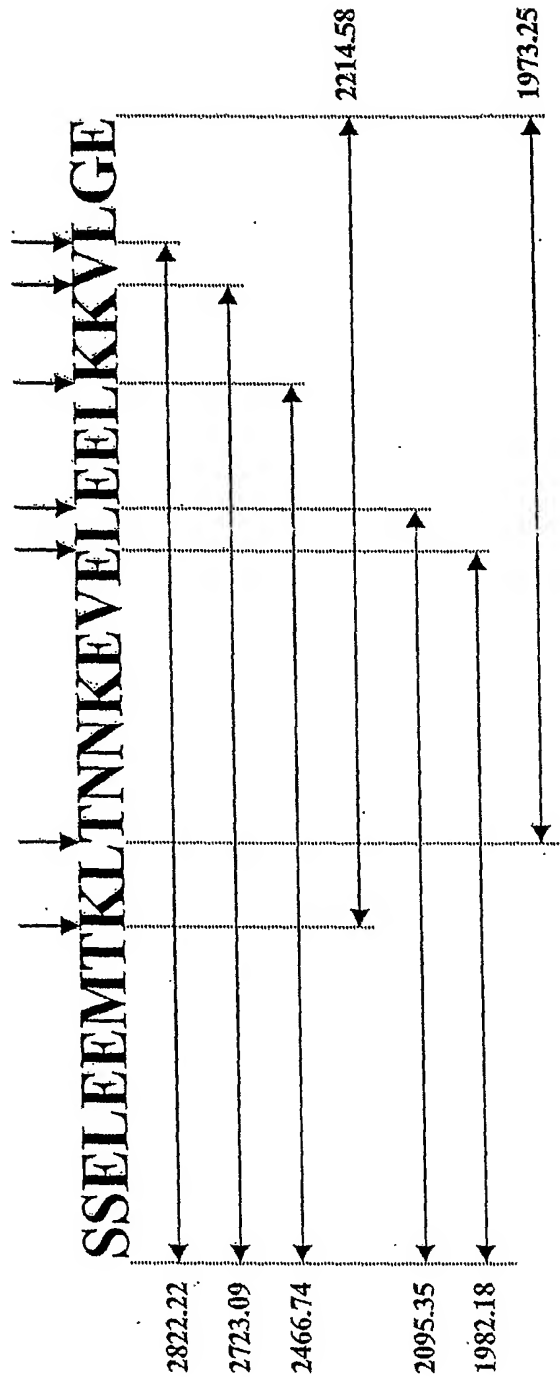


Figure 57

SCP-1 (518-545)

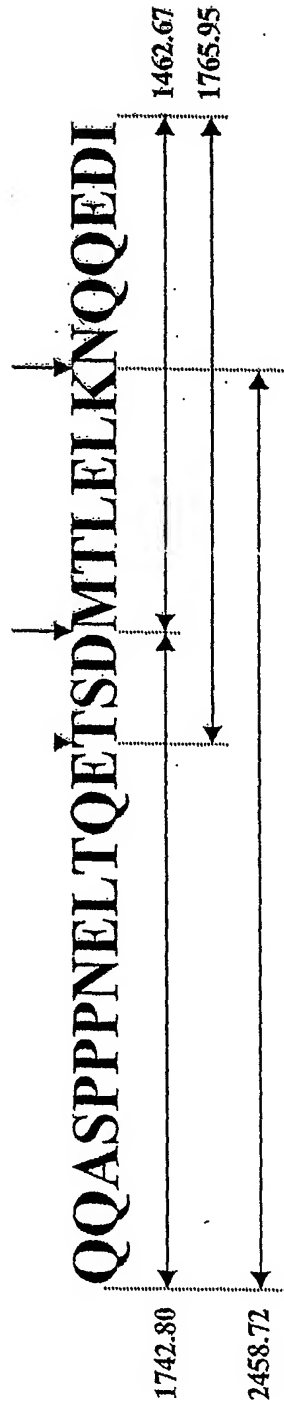


Figure 58

SCP-1 (545-578)

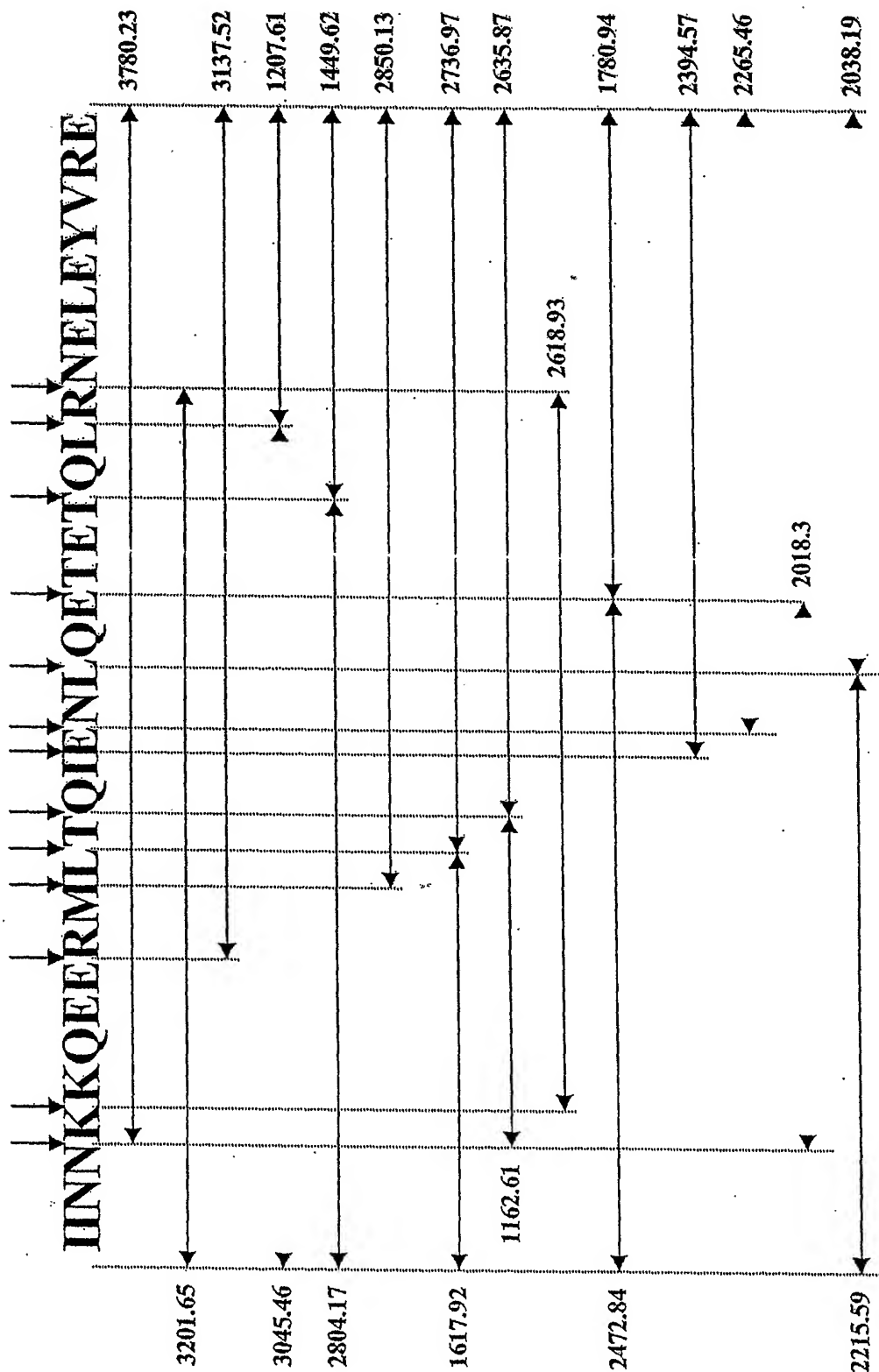


Figure 59

SCP-1 (559-585)

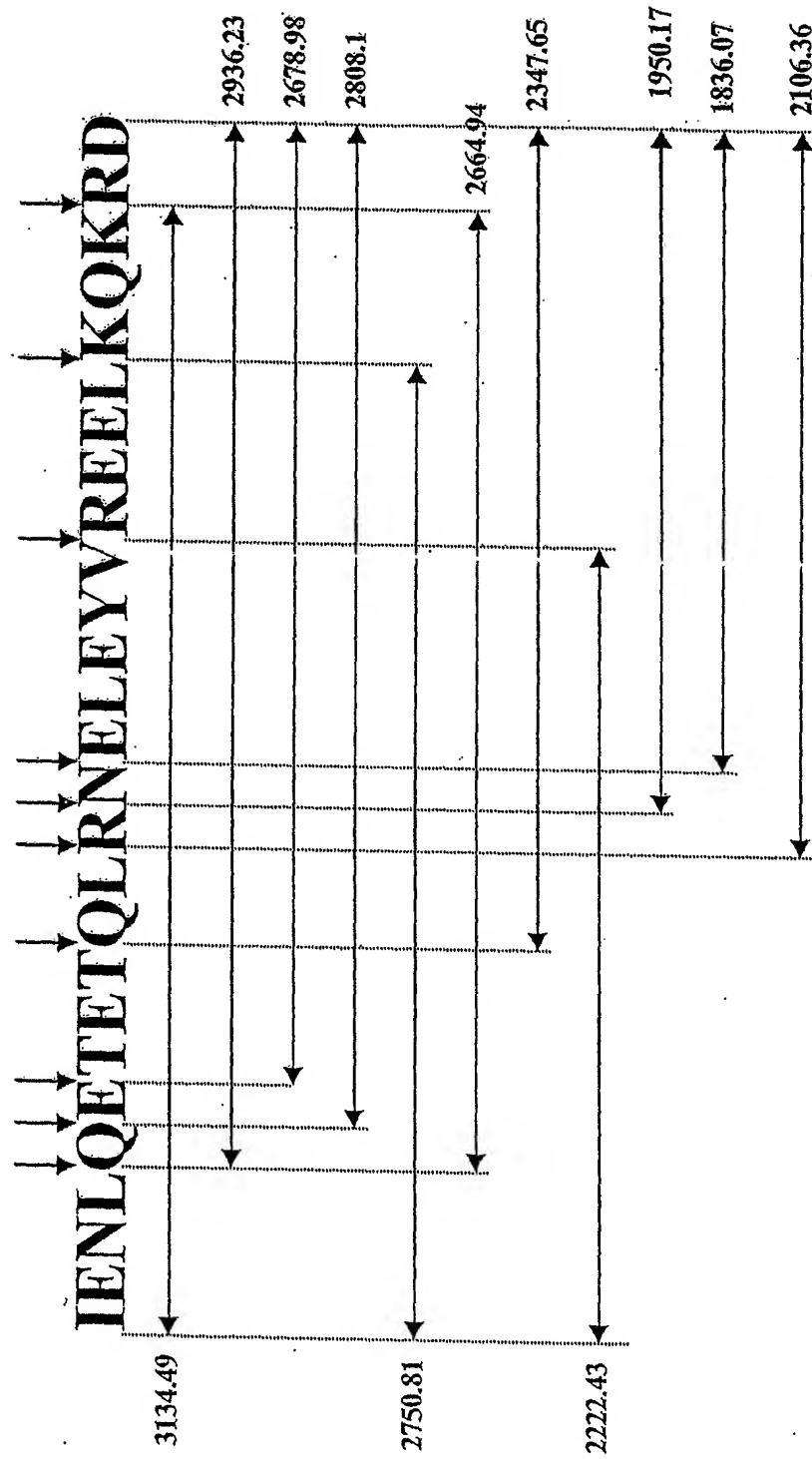


Figure 60

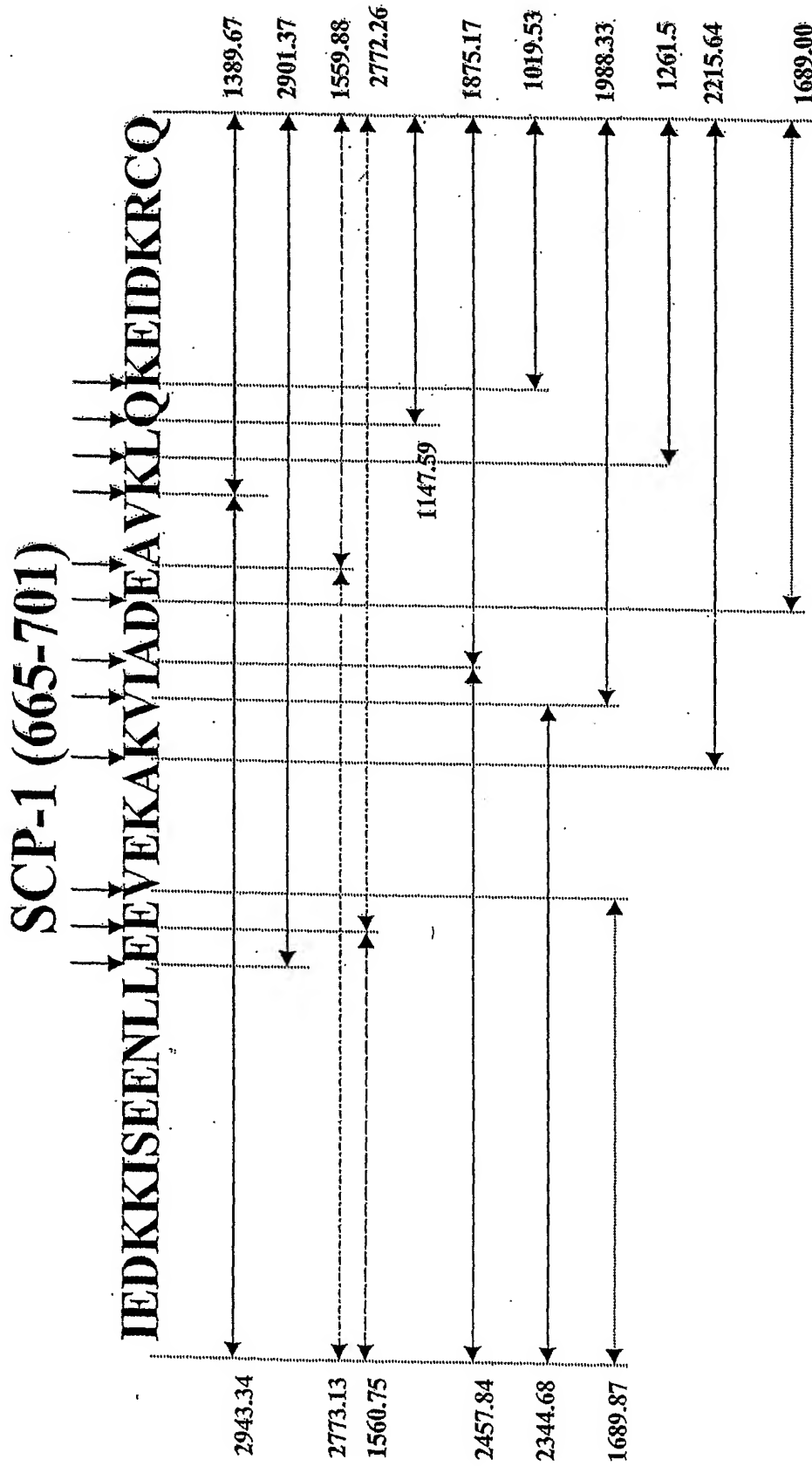


Figure 61

SCP-1 (694-720)

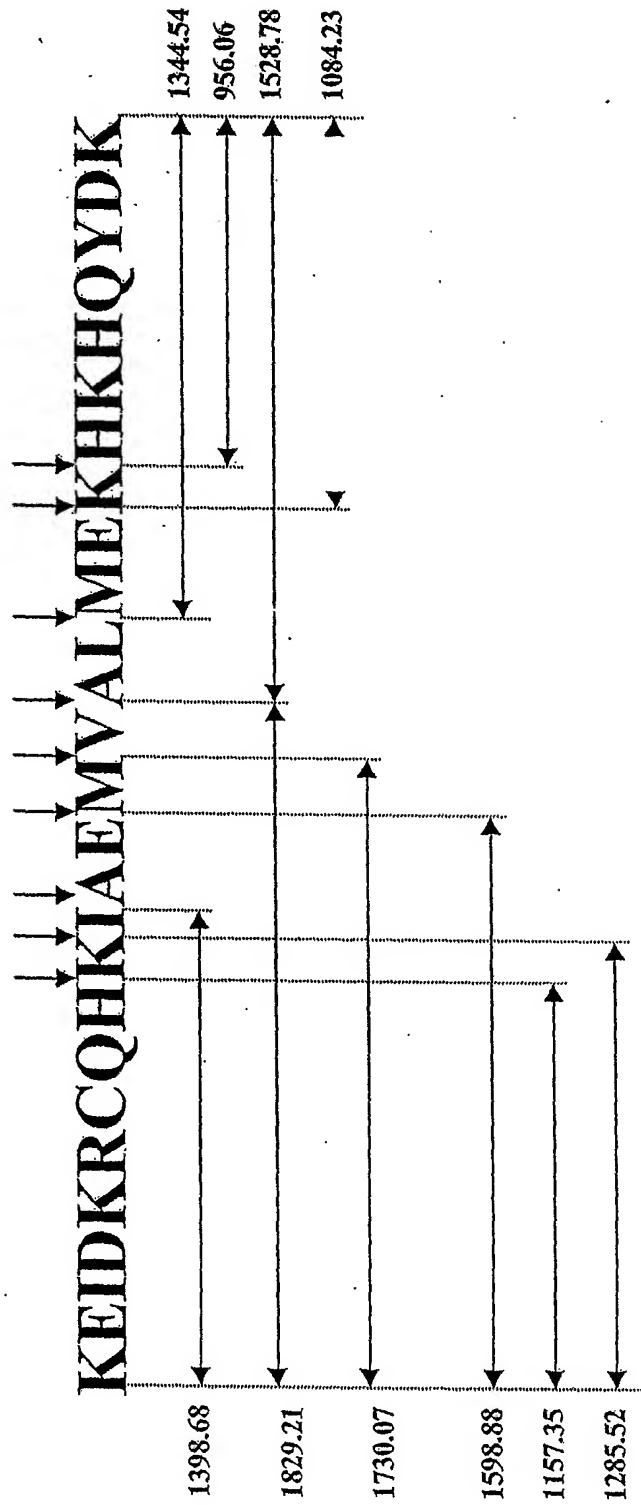


Figure 62

SCP-1 735-769

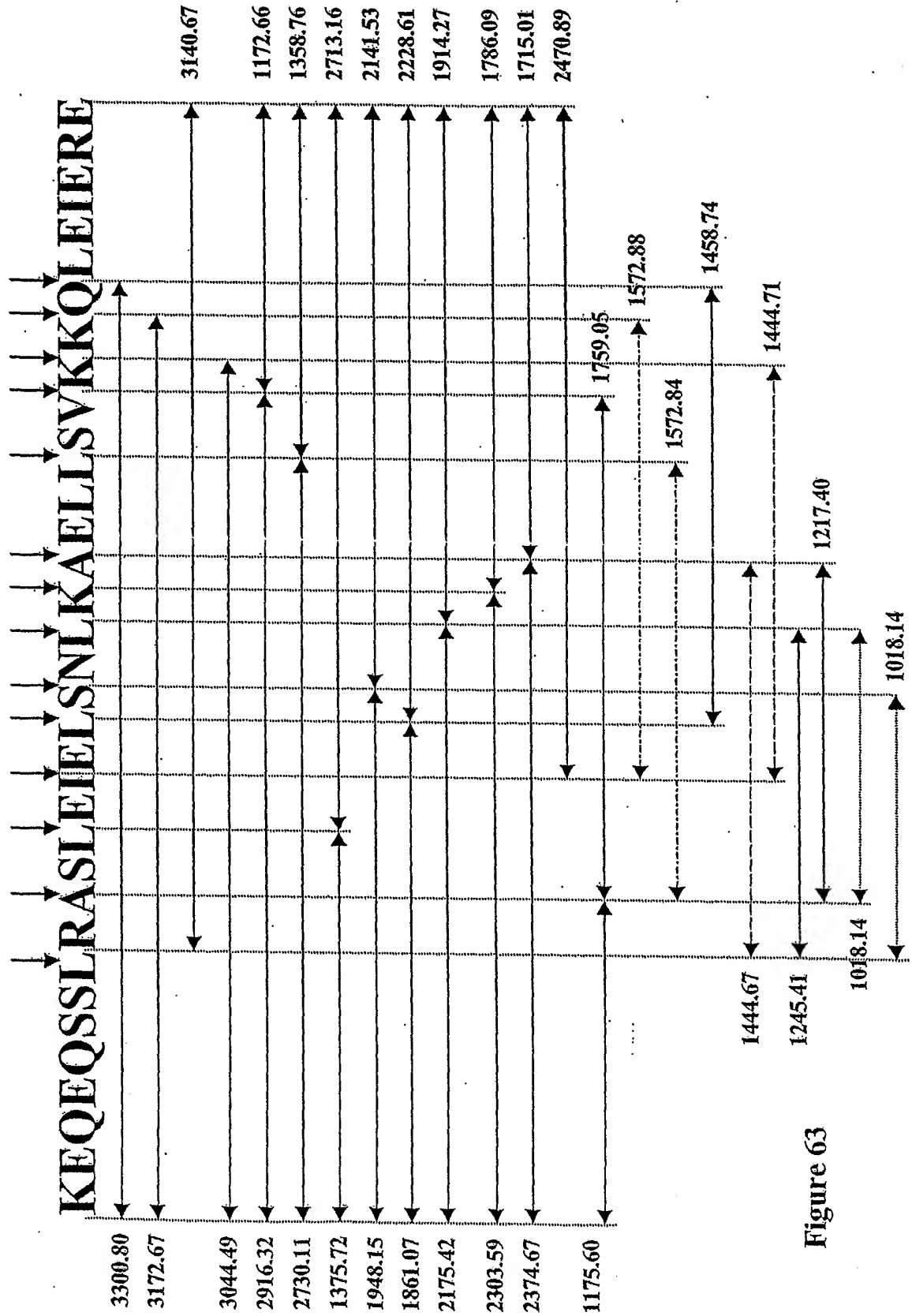


Figure 63

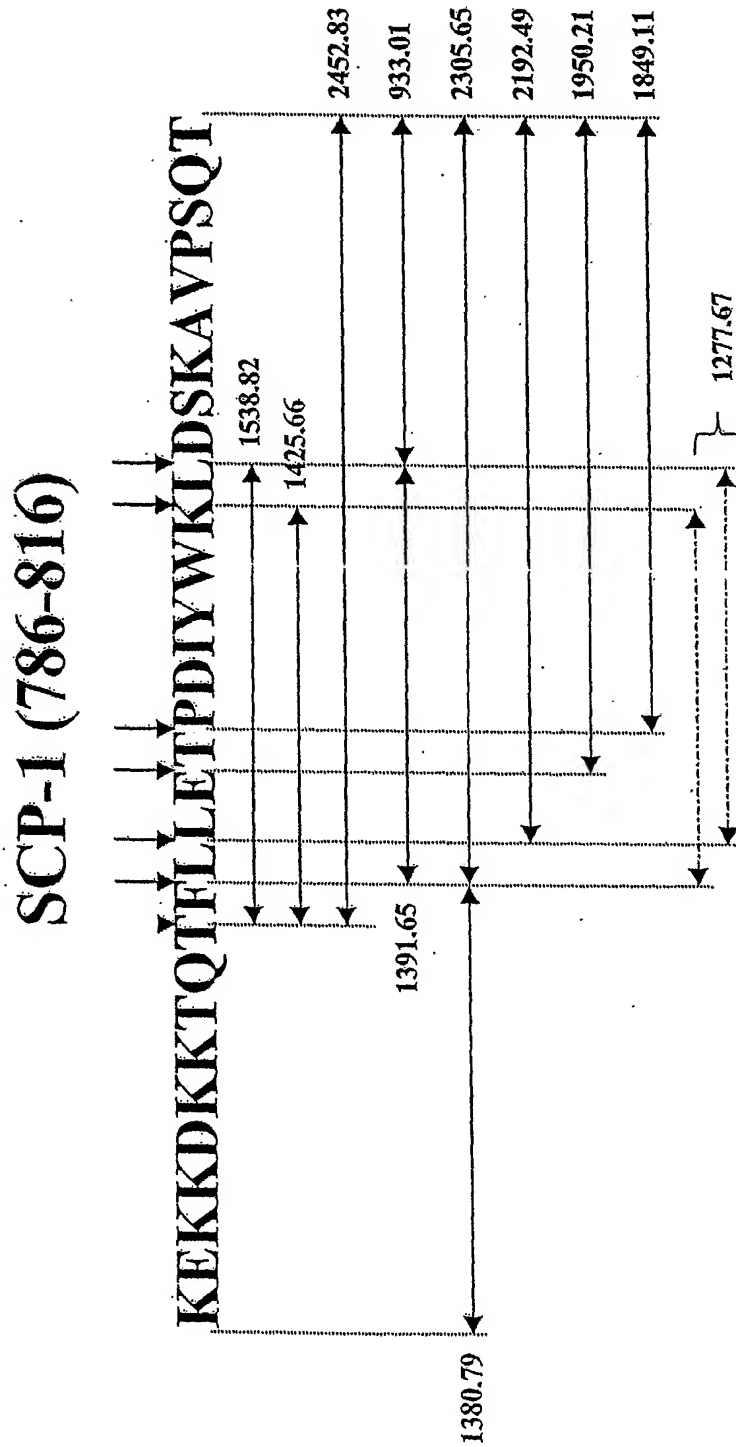


Figure 64

SCP-1 (806-833)

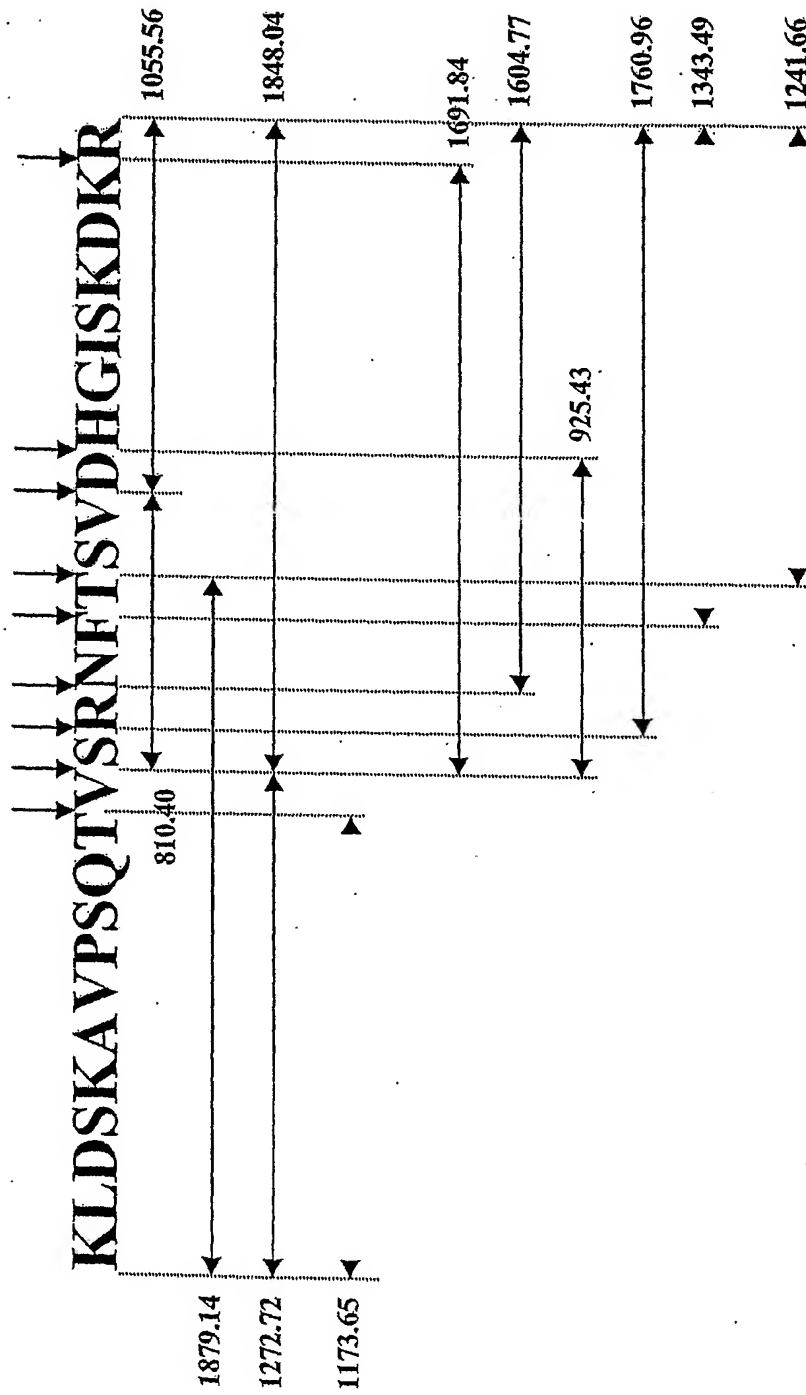


Figure 65

SCP-1 (826-853)

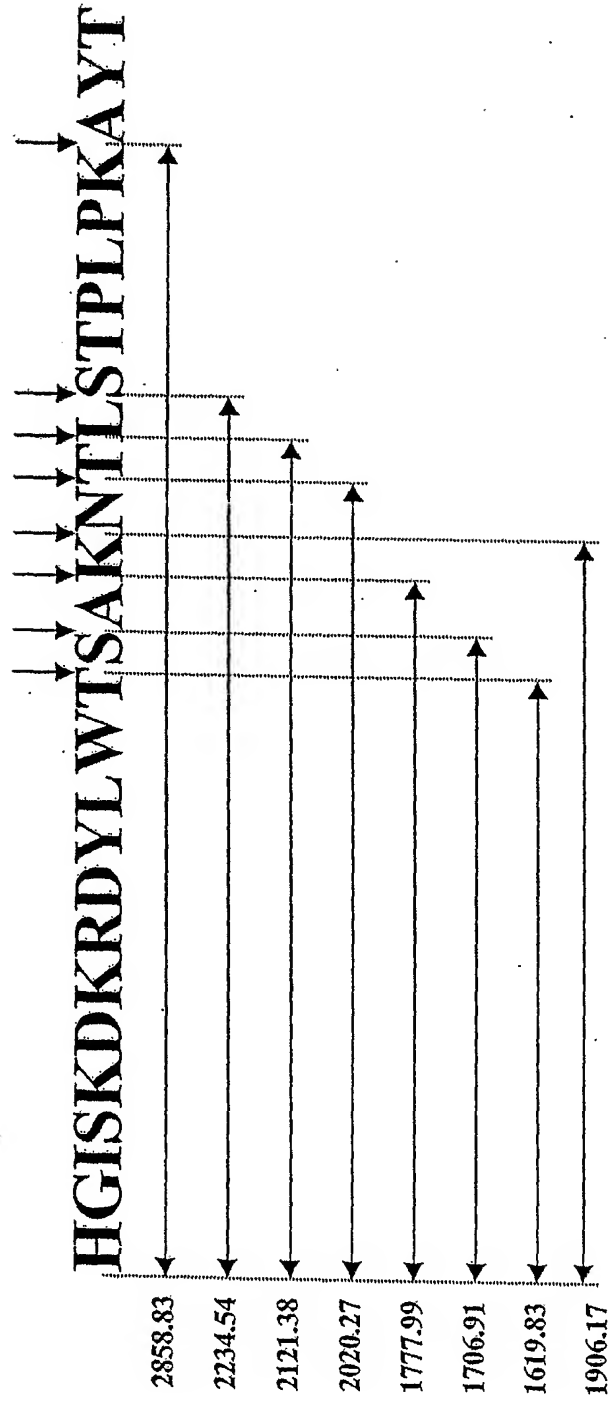


Figure 66

SCP-1 (832-859)

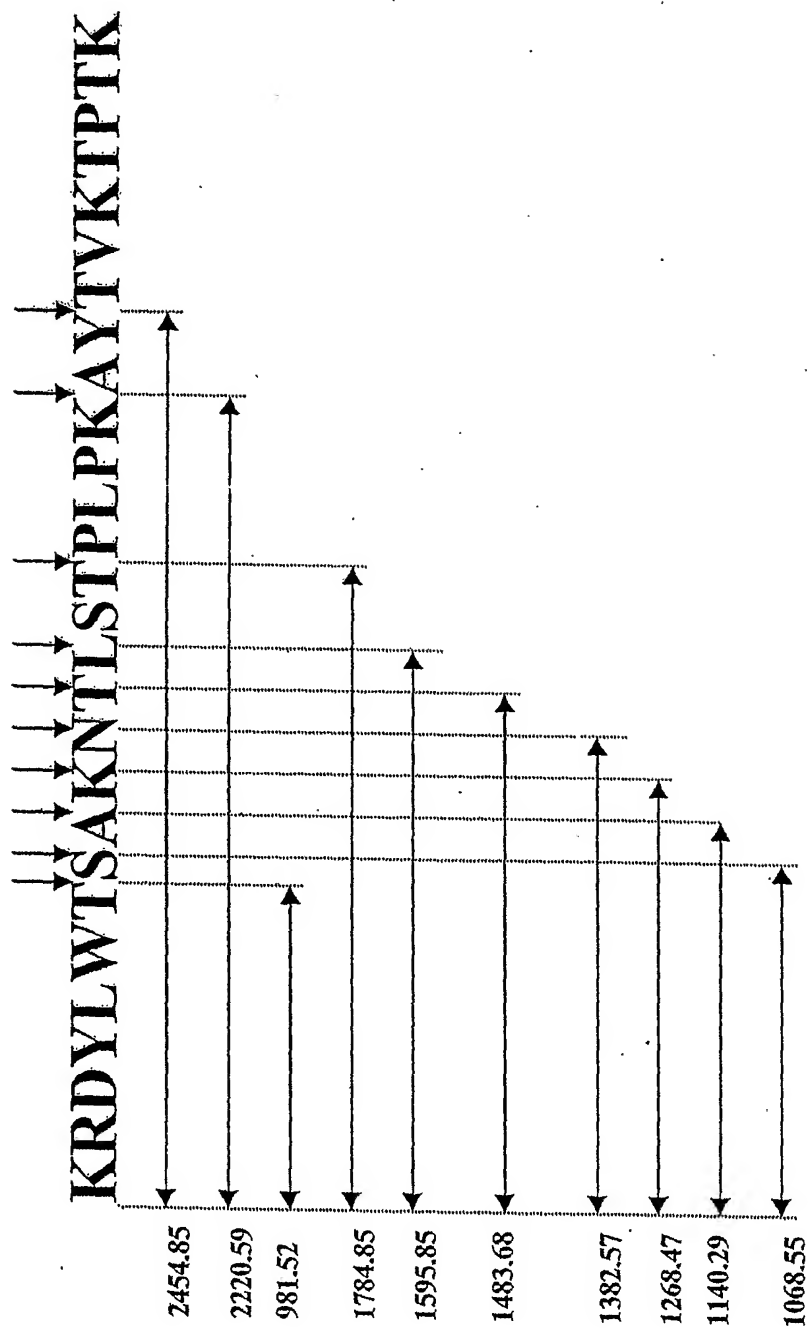


Figure 67

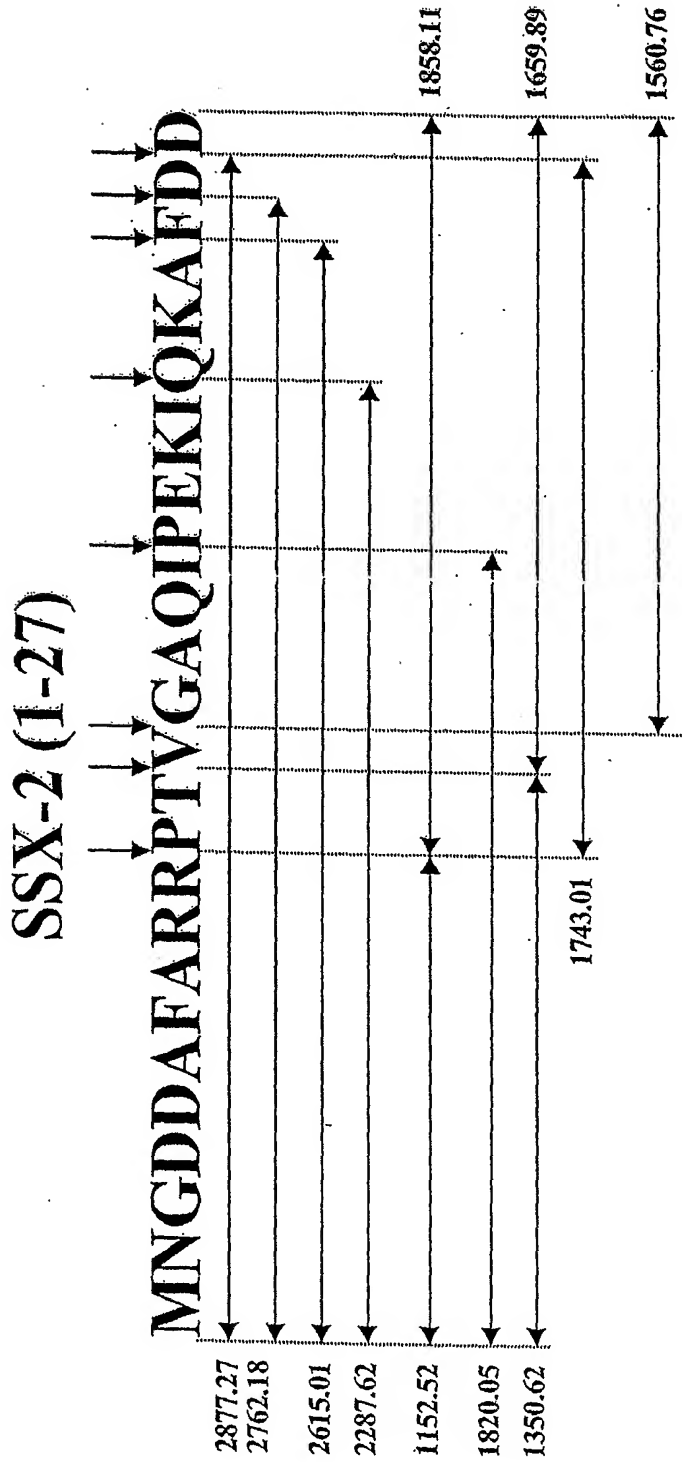


Figure 68

Survivin (116-142)

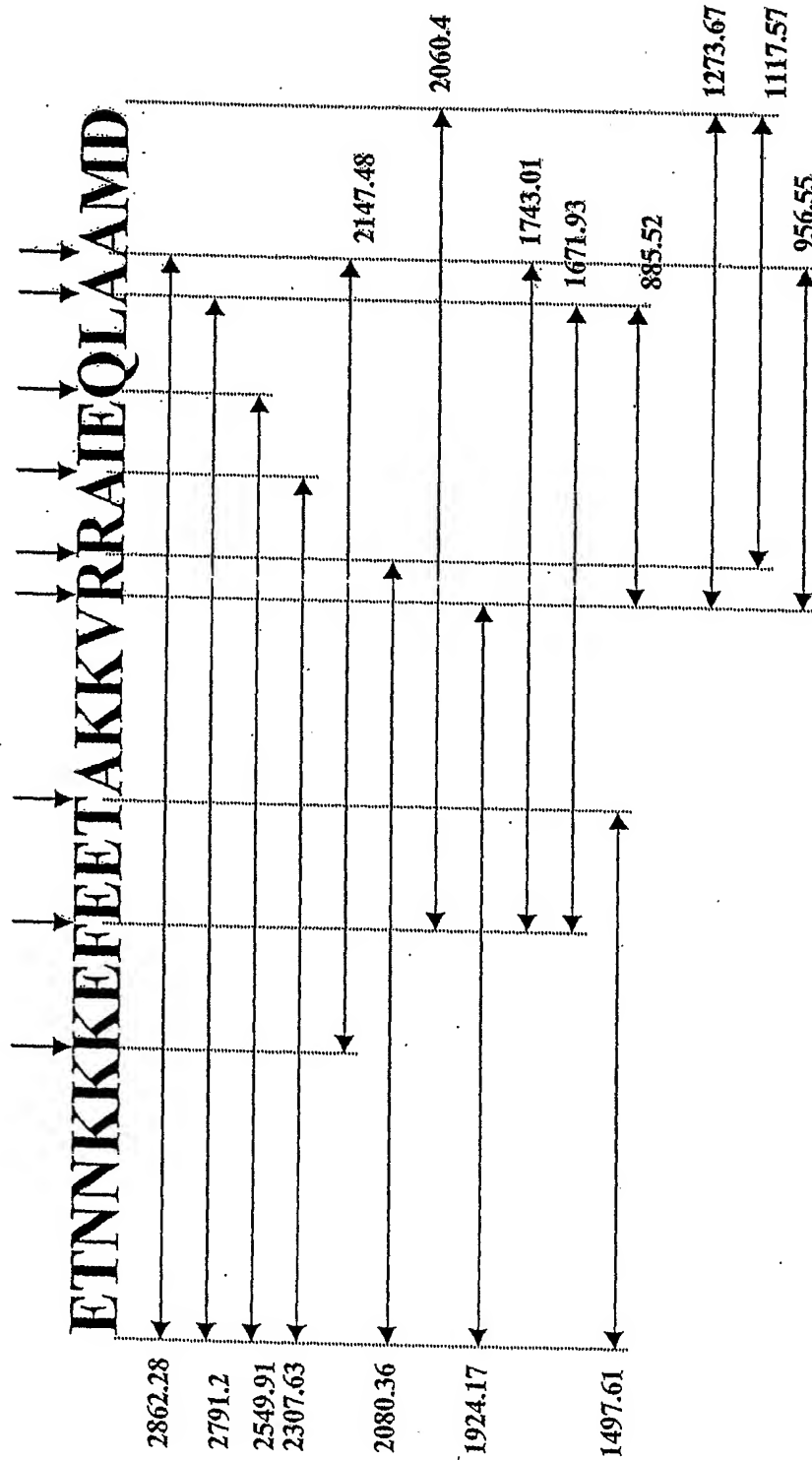


Figure 69

BAGE (1-35)

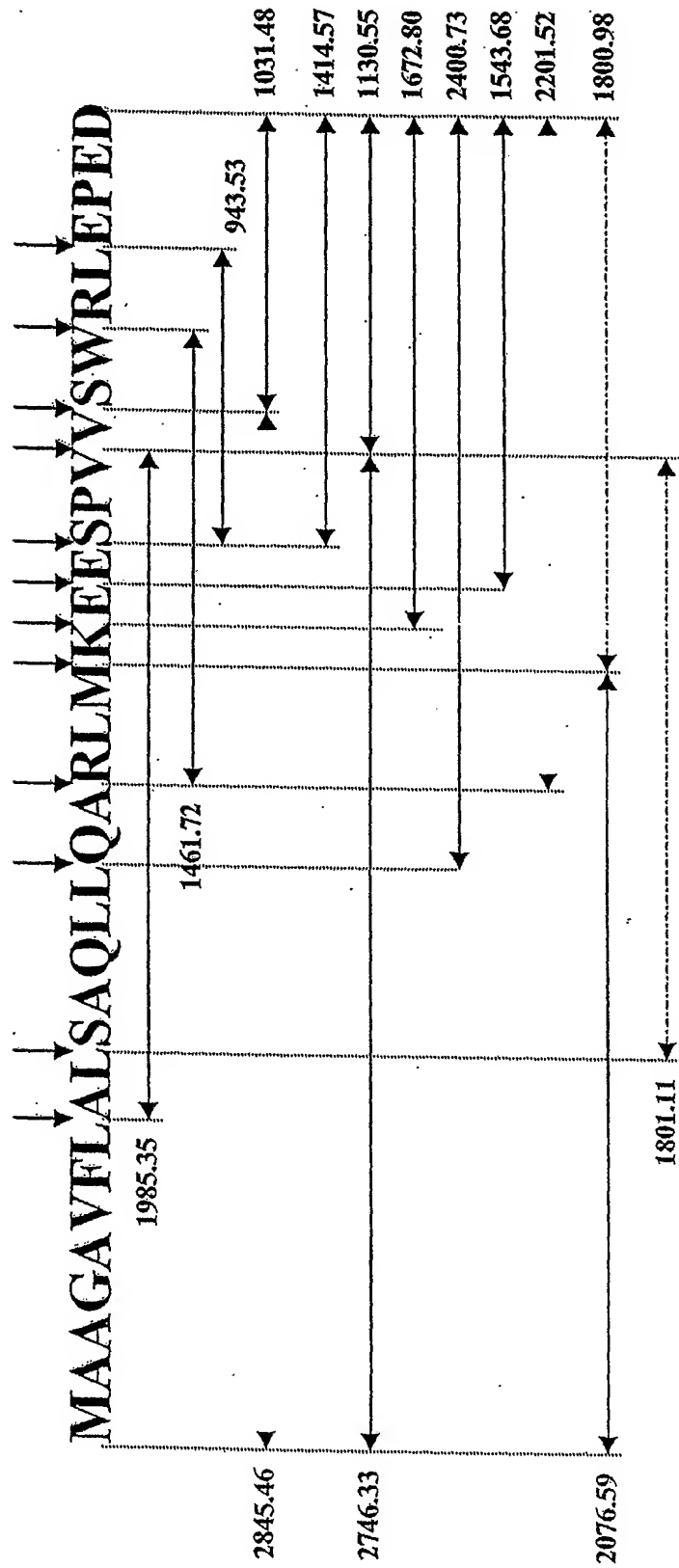


Figure 70

SEQUENCE LISTING

<110> MANNKIND CORPORATION
 SIMARD, John J. L.
 DIAMOND, David C.
 LIU, Liping
 LIU, Zheng

<120> EPITOPE SEQUENCES

<130> MANNK.032VPC

<150> US 60/409123

<151> 2002-09-06

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|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Met | Leu | Leu | Ala | Val | Leu | Tyr | Cys | Leu | Leu | Trp | Ser | Phe | Gln | Thr | Ser | 1 | 5 | 10 | 15 |
| Ala | Gly | His | Phe | Pro | Arg | Ala | Cys | Val | Ser | Ser | Lys | Asn | Leu | Met | Glu | 20 | 25 | 30 | |
| Lys | Glu | Cys | Cys | Pro | Pro | Trp | Ser | Gly | Asp | Arg | Ser | Pro | Cys | Gly | Gln | 35 | 40 | 45 | |
| Leu | Ser | Gly | Arg | Gly | Ser | Cys | Gln | Asn | Ile | Leu | Leu | Ser | Asn | Ala | Pro | 50 | 55 | 60 | |
| Leu | Gly | Pro | Gln | Phe | Pro | Phe | Thr | Gly | Val | Asp | Asp | Arg | Glu | Ser | Trp | 65 | 70 | 75 | 80 |
| Pro | Ser | Val | Phe | Tyr | Asn | Arg | Thr | Cys | Gln | Cys | Ser | Gly | Asn | Phe | Met | 85 | 90 | 95 | |
| Gly | Phe | Asn | Cys | Gly | Asn | Cys | Lys | Phe | Gly | Phe | Trp | Gly | Pro | Asn | Cys | 100 | 105 | 110 | |
| Thr | Glu | Arg | Arg | Leu | Leu | Val | Arg | Arg | Asn | Ile | Phe | Asp | Leu | Ser | Ala | 115 | 120 | 125 | |
| Pro | Glu | Lys | Asp | Lys | Phe | Phe | Ala | Tyr | Leu | Thr | Leu | Ala | Lys | His | Thr | 130 | 135 | 140 | |
| Ile | Ser | Ser | Asp | Tyr | Val | Ile | Pro | Ile | Gly | Thr | Tyr | Gly | Gln | Met | Lys | 145 | 150 | 155 | 160 |
| Asn | Gly | Ser | Thr | Pro | Met | Phe | Asn | Asp | Ile | Asn | Ile | Tyr | Asp | Leu | Phe | 165 | 170 | 175 | |
| Val | Trp | Met | His | Tyr | Tyr | Val | Ser | Met | Asp | Ala | Leu | Leu | Gly | Gly | Ser | 180 | 185 | 190 | |

Glu Ile Trp Arg Asp Ile Asp Phe Ala His Glu Ala Pro Ala Phe Leu
 195 200 205
 Pro Trp His Arg Leu Phe Leu Leu Arg Trp Glu Gln Glu Ile Gln Lys
 210 215 220
 Leu Thr Gly Asp Glu Asn Phe Thr Ile Pro Tyr Trp Asp Trp Arg Asp
 225 230 235 240
 Ala Glu Lys Cys Asp Ile Cys Thr Asp Glu Tyr Met Gly Gly Gln His
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 Pro Thr Asn Pro Asn Leu Leu Ser Pro Ala Ser Phe Phe Ser Ser Trp
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 Gln Ile Val Cys Ser Arg Leu Glu Tyr Asn Ser His Gln Ser Leu
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 Cys Leu Ser Leu Thr Gln Tyr Glu Ser Gly Ser Met Asp Lys Ala Ala
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 Gly Ile Ala Asp Ala Ser Gln Ser Met His Asn Ala Leu His Ile
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 Ile Phe Leu Leu His His Ala Phe Val Asp Ser Ile Phe Glu Gln Trp
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 Leu Arg Arg His Arg Pro Leu Gln Glu Val Tyr Pro Glu Ala Asn Ala
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 Pro Ile Gly His Asn Arg Glu Ser Tyr Met Val Pro Phe Ile Pro Leu
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 Tyr Arg Asn Gly Asp Phe Phe Ile Ser Ser Lys Asp Leu Gly Tyr Asp
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 Tyr Ser Tyr Leu Gln Asp Ser Asp Pro Asp Ser Phe Gln Asp Tyr Ile
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 Lys Ser Tyr Leu Glu Gln Ala Ser Arg Ile Trp Ser Trp Leu Leu Gly
 465 470 475 480
 Ala Ala Met Val Gly Ala Val Leu Thr Ala Leu Leu Ala Gly Leu Val
 485 490 495
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 Pro Leu Leu Met Glu Lys Glu Asp Tyr His Ser Leu Tyr Gln Ser His
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<210> 3

<211> 188

<212> PRT

<213> Homo sapiens

<400> 3

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 35 40 45
 Val Tyr Met Lys Arg Lys Tyr Glu Ala Met Thr Lys Leu Gly Phe Lys
 50 55 60
 Ala Thr Leu Pro Pro Phe Met Cys Asn Lys Arg Ala Glu Asp Phe Gln

| | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|---------|
| 65 | | | | | 70 | | | | | 75 | | | | 80 |
| Gly | Asn | Asp | Leu | Asp | Asn | Asp | Pro | Asn | Arg | Gly | Asn | Gln | Val | Glu Arg |
| | | | | 85 | | | | | 90 | | | | | 95 |
| Pro | Gln | Met | Thr | Phe | Gly | Arg | Leu | Gln | Gly | Ile | Ser | Pro | Lys | Ile Met |
| | | | 100 | | | | | 105 | | | | | 110 | |
| Pro | Lys | Lys | Pro | Ala | Glu | Glu | Gly | Asn | Asp | Ser | Glu | Glu | Val | Pro Glu |
| | | 115 | | | | | 120 | | | | | 125 | | |
| Ala | Ser | Gly | Pro | Gln | Asn | Asp | Gly | Lys | Glu | Leu | Cys | Pro | Pro | Gly Lys |
| | 130 | | | | | 135 | | | | | 140 | | | |
| Pro | Thr | Thr | Ser | Glu | Lys | Ile | His | Glu | Arg | Ser | Gly | Pro | Lys | Arg Gly |
| 145 | | | | | 150 | | | | | 155 | | | | 160 |
| Glu | His | Ala | Trp | Thr | His | Arg | Leu | Arg | Glu | Arg | Lys | Gln | Leu | Val Ile |
| | | | 165 | | | | | 170 | | | | | 175 | |
| Tyr | Glu | Glu | Ile | Ser | Asp | Pro | Glu | Glu | Asp | Asp | Glu | | | |
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<210> 4

<211> 750

<212> PRT

<213> Homo sapiens

<400> 4

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| 1 | | | | 5 | | | | 10 | | | | | | 15 | |
| Arg | Pro | Arg | Trp | Leu | Cys | Ala | Gly | Ala | Leu | Val | Leu | Ala | Gly | Gly | Phe |
| | | | 20 | | | | | 25 | | | | | 30 | | |
| Phe | Leu | Leu | Gly | Phe | Leu | Phe | Gly | Trp | Phe | Ile | Lys | Ser | Ser | Asn | Glu |
| | 35 | | | | | | 40 | | | | 45 | | | | |
| Ala | Thr | Asn | Ile | Thr | Pro | Lys | His | Asn | Met | Lys | Ala | Phe | Leu | Asp | Glu |
| | 50 | | | | | 55 | | | | 60 | | | | | |
| Leu | Lys | Ala | Glu | Asn | Ile | Lys | Lys | Phe | Leu | Tyr | Asn | Phe | Thr | Gln | Ile |
| 65 | | | | | 70 | | | | | 75 | | | | 80 | |
| Pro | His | Leu | Ala | Gly | Thr | Glu | Gln | Asn | Phe | Gln | Leu | Ala | Lys | Gln | Ile |
| | | | 85 | | | | | 90 | | | | | 95 | | |
| Gln | Ser | Gln | Trp | Lys | Glu | Phe | Gly | Leu | Asp | Ser | Val | Glu | Leu | Ala | His |
| | | | 100 | | | | | 105 | | | | | 110 | | |
| Tyr | Asp | Val | Leu | Leu | Ser | Tyr | Pro | Asn | Lys | Thr | His | Pro | Asn | Tyr | Ile |
| | 115 | | | | | 120 | | | | | | 125 | | | |
| Ser | Ile | Ile | Asn | Glu | Asp | Gly | Asn | Glu | Ile | Phe | Asn | Thr | Ser | Leu | Phe |
| | 130 | | | | | 135 | | | | | 140 | | | | |
| Glu | Pro | Pro | Pro | Pro | Gly | Tyr | Glu | Asn | Val | Ser | Asp | Ile | Val | Pro | Pro |
| 145 | | | | | 150 | | | | | 155 | | | | 160 | |
| Phe | Ser | Ala | Phe | Ser | Pro | Gln | Gly | Met | Pro | Glu | Gly | Asp | Leu | Val | Tyr |
| | | | 165 | | | | | 170 | | | | | 175 | | |
| Val | Asn | Tyr | Ala | Arg | Thr | Glu | Asp | Phe | Lys | Leu | Glu | Arg | Asp | Met | |
| | 180 | | | | | | 185 | | | | | 190 | | | |
| Lys | Ile | Asn | Cys | Ser | Gly | Lys | Ile | Val | Ile | Ala | Arg | Tyr | Gly | Lys | Val |
| | 195 | | | | | 200 | | | | | | 205 | | | |
| Phe | Arg | Gly | Asn | Lys | Val | Lys | Asn | Ala | Gln | Leu | Ala | Gly | Ala | Lys | Gly |
| | 210 | | | | | 215 | | | | | 220 | | | | |
| Val | Ile | Leu | Tyr | Ser | Asp | Pro | Ala | Asp | Tyr | Phe | Ala | Pro | Gly | Val | Lys |
| 225 | | | | 230 | | | | | 235 | | | | | 240 | |
| Ser | Tyr | Pro | Asp | Gly | Trp | Asn | Leu | Pro | Gly | Gly | Gly | Val | Gln | Arg | Gly |
| | | | 245 | | | | | 250 | | | | | 255 | | |
| Asn | Ile | Leu | Asn | Leu | Asn | Gly | Ala | Gly | Asp | Pro | Leu | Thr | Pro | Gly | Tyr |
| | | 260 | | | | 265 | | | | | | 270 | | | |
| Pro | Ala | Asn | Glu | Tyr | Ala | Tyr | Arg | Arg | Gly | Ile | Ala | Glu | Ala | Val | Gly |
| | 275 | | | | | 280 | | | | | 285 | | | | |
| Leu | Pro | Ser | Ile | Pro | Val | His | Pro | Ile | Gly | Tyr | Tyr | Asp | Ala | Gln | Lys |
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 Gly Ser Leu Lys Val Pro Tyr Asn Val Gly Pro Gly Phe Thr Gly Asn
 325 330 335
 Phe Ser Thr Gln Lys Val Lys Met His Ile His Ser Thr Asn Glu Val
 340 345 350
 Thr Arg Ile Tyr Asn Val Ile Gly Thr Leu Arg Gly Ala Val Glu Pro
 355 360 365
 Asp Arg Tyr Val Ile Leu Gly Gly His Arg Asp Ser Trp Val Phe Gly
 370 375 380
 Gly Ile Asp Pro Gln Ser Gly Ala Ala Val Val His Glu Ile Val Arg
 385 390 395 400
 Ser Phe Gly Thr Leu Lys Lys Glu Gly Trp Arg Pro Arg Arg Thr Ile
 405 410 415
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 435 440 445
 Tyr Ile Asn Ala Asp Ser Ser Ile Glu Gly Asn Tyr Thr Leu Arg Val
 450 455 460
 Asp Cys Thr Pro Leu Met Tyr Ser Leu Val His Asn Leu Thr Lys Glu
 465 470 475 480
 Leu Lys Ser Pro Asp Glu Gly Phe Glu Gly Lys Ser Leu Tyr Glu Ser
 485 490 495
 Trp Thr Lys Lys Ser Pro Ser Pro Glu Phe Ser Gly Met Pro Arg Ile
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 Ser Lys Leu Gly Ser Gly Asn Asp Phe Glu Val Phe Phe Gln Arg Leu
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 Gly Ile Ala Ser Gly Arg Ala Arg Tyr Thr Lys Asn Trp Glu Thr Asn
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 Leu Val Glu Lys Phe Tyr Asp Pro Met Phe Lys Tyr His Leu Thr Val
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 Ala Gln Val Arg Gly Gly Met Val Phe Glu Leu Ala Asn Ser Ile Val
 580 585 590
 Leu Pro Phe Asp Cys Arg Asp Tyr Ala Val Val Leu Arg Lys Tyr Ala
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 Asp Lys Ile Tyr Ser Ile Ser Met Lys His Pro Gln Glu Met Lys Thr
 610 615 620
 Tyr Ser Val Ser Phe Asp Ser Leu Phe Ser Ala Val Lys Asn Phe Thr
 625 630 635 640
 Glu Ile Ala Ser Lys Phe Ser Glu Arg Leu Gln Asp Phe Asp Lys Ser
 645 650 655
 Asn Pro Ile Val Leu Arg Met Met Asn Asp Gln Leu Met Phe Leu Glu
 660 665 670
 Arg Ala Phe Ile Asp Pro Leu Gly Leu Pro Asp Arg Pro Phe Tyr Arg
 675 680 685
 His Val Ile Tyr Ala Pro Ser Ser His Asn Lys Tyr Ala Gly Glu Ser
 690 695 700
 Phe Pro Gly Ile Tyr Asp Ala Leu Phe Asp Ile Glu Ser Lys Val Asp
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<211> 1964

<212> DNA

<213> Homo sapiens

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<212> PRT

<213> Homo sapiens

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<212> PRT

<213> Homo sapiens

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Phe Lys Ala Thr Leu Pro
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 <212> PRT
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<400> 32
 Met Pro Glu Gly Asp Leu Val Tyr Val
 1 5

<210> 33
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<400> 33
Gly Met Pro Glu Gly Asp Leu Val Tyr Val
1 5 10

<210> 34
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<400> 34
Gly Met Pro Glu Gly Asp Leu Val Tyr
1 5

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<400> 35
Gln Gly Met Pro Glu Gly Asp Leu Val Tyr
1 5 10

<210> 36
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<400> 36
Met Pro Glu Gly Asp Leu Val Tyr
1 5

<210> 37
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<400> 37
Glu Gly Asp Leu Val Tyr Val Asn Tyr
1 5

<210> 38
<211> 10
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<213> Homo sapiens

<400> 38
Pro Glu Gly Asp Leu Val Tyr Val Asn Tyr
1 5 10

<210> 39
<211> 10
<212> PRT
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<400> 39
Leu Val Tyr Val Asn Tyr Ala Arg Thr Glu
1 5 10

<210> 40
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<212> PRT
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<400> 40
Val Asn Tyr Ala Arg Thr Glu Asp Phe
1 5

<210> 41
<211> 10
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<400> 41
Tyr Val Asn Tyr Ala Arg Thr Glu Asp Phe
1 5 10

<210> 42
<211> 9
<212> PRT
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<400> 42
Asn Tyr Ala Arg Thr Glu Asp Phe Phe
1 5

<210> 43
<211> 8
<212> PRT
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<400> 43
Tyr Ala Arg Thr Glu Asp Phe Phe
1 5

<210> 44
<211> 9
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<400> 44
Arg Thr Glu Asp Phe Phe Lys Leu Glu
1 5

<210> 45

<211> 30
 <212> PRT
 <213> Homo sapiens

<400> 45
 Arg Gly Ile Ala Glu Ala Val Gly Leu Pro Ser Ile Pro Val His Pro
 1 5 10 15
 Ile Gly Tyr Tyr Asp Ala Gln Lys Leu Leu Glu Lys Met Gly
 20 25 30

<210> 46
 <211> 25
 <212> PRT
 <213> Homo sapiens

<400> 46
 Ile Ala Glu Ala Val Gly Leu Pro Ser Ile Pro Val His Pro Ile Gly
 1 5 10 15
 Tyr Tyr Asp Ala Gln Lys Leu Leu Glu
 20 25

<210> 47
 <211> 9
 <212> PRT
 <213> Homo sapiens

<400> 47
 Leu Pro Ser Ile Pro Val His Pro Ile
 1 5

<210> 48
 <211> 10
 <212> PRT
 <213> Homo sapiens

<400> 48
 Gly Leu Pro Ser Ile Pro Val His Pro Ile
 1 5 10

<210> 49
 <211> 9
 <212> PRT
 <213> Homo sapiens

<400> 49
 Ile Gly Tyr Tyr Asp Ala Gln Lys Leu
 1 5

<210> 50
 <211> 10
 <212> PRT
 <213> Homo sapiens

<400> 50
 Pro Ile Gly Tyr Tyr Asp Ala Gln Lys Leu
 1 5 10

<210> 51
 <211> 9
 <212> PRT
 <213> Homo sapiens

<400> 51
 Ser Ile Pro Val His Pro Ile Gly Tyr
 1 5

<210> 52
 <211> 10
 <212> PRT
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<400> 52
 Pro Ser Ile Pro Val His Pro Ile Gly Tyr
 1 5 10

<210> 53
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<400> 53
 Ile Pro Val His Pro Ile Gly Tyr
 1 5

<210> 54
 <211> 9
 <212> PRT
 <213> Homo sapiens

<400> 54
 Tyr Tyr Asp Ala Gln Lys Leu Leu Glu
 1 5

<210> 55
 <211> 27
 <212> PRT
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<400> 55
 Ser Ser Ile Glu Gly Asn Tyr Thr Leu Arg Val Asp Cys Thr Pro Leu
 1 5 10 15
 Met Tyr Ser Leu Val His Leu Thr Lys Glu Leu
 20 25

<210> 56
 <211> 9
 <212> PRT
 <213> Homo sapiens

<400> 56
 Ile Glu Gly Asn Tyr Thr Leu Arg Val

1 5

<210> 57
<211> 10
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<213> Homo sapiens

<400> 57
Ser Ile Glu Gly Asn Tyr Thr Leu Arg Val
1 5 10

<210> 58
<211> 8
<212> PRT
<213> Homo sapiens

<400> 58
Glu Gly Asn Tyr Thr Leu Arg Val
1 5

<210> 59
<211> 9
<212> PRT
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<400> 59
Thr Leu Arg Val Asp Cys Thr Pro Leu
1 5

<210> 60
<211> 10
<212> PRT
<213> Homo sapiens

<400> 60
Tyr Thr Leu Arg Val Asp Cys Thr Pro Leu
1 5 10

<210> 61
<211> 9
<212> PRT
<213> Homo sapiens

<400> 61
Leu Arg Val Asp Cys Thr Pro Leu Met
1 5

<210> 62
<211> 9
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<400> 62
Arg Val Asp Cys Thr Pro Leu Met Tyr
1 5

<210> 63
 <211> 10
 <212> PRT
 <213> Homo sapiens

<400> 63
 Leu Arg Val Asp Cys Thr Pro Leu Met Tyr
 1 5 10

<210> 64
 <211> 35
 <212> PRT
 <213> Homo sapiens

<400> 64
 Phe Asp Lys Ser Asn Pro Ile Val Leu Arg Met Met Asn Asp Gln Leu
 1 5 10 15
 Met Phe Leu Glu Arg Ala Phe Ile Asp Pro Leu Gly Leu Pro Asp Arg
 20 25 30
 Pro Phe Tyr
 35

<210> 65
 <211> 22
 <212> PRT
 <213> Homo sapiens

<400> 65
 Val Leu Arg Met Met Asn Asp Gln Leu Met Phe Leu Glu Arg Ala Phe
 1 5 10 15
 Ile Asp Pro Leu Gly Leu
 20

<210> 66
 <211> 9
 <212> PRT
 <213> Homo sapiens

<400> 66
 Met Met Asn Asp Gln Leu Met Phe Leu
 1 5

<210> 67
 <211> 10
 <212> PRT
 <213> Homo sapiens

<400> 67
 Arg Met Met Asn Asp Gln Leu Met Phe Leu
 1 5 10

<210> 68
 <211> 9
 <212> PRT

<213> Homo sapiens

<400> 68

Arg Met Met Asn Asp Gln Leu Met Phe
 1 5

<210> 69

<211> 17

<212> PRT

<213> Homo sapiens

<400> 69

Met Leu Leu Ala Val Leu Tyr Cys Leu Leu Trp Ser Phe Gln Thr Ser
 1 5 10 15
 Ala

<210> 70

<211> 661

<212> PRT

<213> Homo sapiens

<400> 70

Met Asp Leu Val Leu Lys Arg Cys Leu Leu His Leu Ala Val Ile Gly
 1 5 10 15
 Ala Leu Leu Ala Val Gly Ala Thr Lys Val Pro Arg Asn Gln Asp Trp
 20 25 30
 Leu Gly Val Ser Arg Gln Leu Arg Thr Lys Ala Trp Asn Arg Gln Leu
 35 40 45
 Tyr Pro Glu Trp Thr Glu Ala Gln Arg Leu Asp Cys Trp Arg Gly Gly
 50 55 60
 Gln Val Ser Leu Lys Val Ser Asn Asp Gly Pro Thr Leu Ile Gly Ala
 65 70 75 80
 Asn Ala Ser Phe Ser Ile Ala Leu Asn Phe Pro Gly Ser Gln Lys Val
 85 90 95
 Leu Pro Asp Gly Gln Val Ile Trp Val Asn Asn Thr Ile Ile Asn Gly
 100 105 110
 Ser Gln Val Trp Gly Gly Gln Pro Val Tyr Pro Gln Glu Thr Asp Asp
 115 120 125
 Ala Cys Ile Phe Pro Asp Gly Gly Pro Cys Pro Ser Gly Ser Trp Ser
 130 135 140
 Gln Lys Arg Ser Phe Val Tyr Val Trp Lys Thr Trp Gly Gln Tyr Trp
 145 150 155 160
 Gln Val Leu Gly Gly Pro Val Ser Gly Leu Ser Ile Gly Thr Gly Arg
 165 170 175
 Ala Met Leu Gly Thr His Thr Met Glu Val Thr Val Tyr His Arg Arg
 180 185 190
 Gly Ser Arg Ser Tyr Val Pro Leu Ala His Ser Ser Ser Ala Phe Thr
 195 200 205
 Ile Thr Asp Gln Val Pro Phe Ser Val Ser Val Ser Gln Leu Arg Ala
 210 215 220
 Leu Asp Gly Gly Asn Lys His Phe Leu Arg Asn Gln Pro Leu Thr Phe
 225 230 235 240
 Ala Leu Gln Leu His Asp Pro Ser Gly Tyr Leu Ala Glu Ala Asp Leu
 245 250 255
 Ser Tyr Thr Trp Asp Phe Gly Asp Ser Ser Gly Thr Leu Ile Ser Arg
 260 265 270
 Ala Pro Val Val Thr His Thr Tyr Leu Glu Pro Gly Pro Val Thr Ala
 275 280 285

Gln Val Val Leu Gln Ala Ala Ile Pro Leu Thr Ser Cys Gly Ser Ser
 290 295 300
 Pro Val Pro Gly Thr Thr Asp Gly His Arg Pro Thr Ala Glu Ala Pro
 305 310 315 320
 Asn Thr Thr Ala Gly Gln Val Pro Thr Thr Glu Val Val Gly Thr Thr
 325 330 335
 Pro Gly Gln Ala Pro Thr Ala Glu Pro Ser Gly Thr Thr Ser Val Gln
 340 345 350
 Val Pro Thr Thr Glu Val Ile Ser Thr Ala Pro Val Gln Met Pro Thr
 355 360 365
 Ala Glu Ser Thr Gly Met Thr Pro Glu Lys Val Pro Val Ser Glu Val
 370 375 380
 Met Gly Thr Thr Leu Ala Glu Met Ser Thr Pro Glu Ala Thr Gly Met
 385 390 395 400
 Thr Pro Ala Glu Val Ser Ile Val Val Leu Ser Gly Thr Thr Ala Ala
 405 410 415
 Gln Val Thr Thr Thr Glu Trp Val Glu Thr Thr Ala Arg Glu Leu Pro
 420 425 430
 Ile Pro Glu Pro Glu Gly Pro Asp Ala Ser Ser Ile Met Ser Thr Glu
 435 440 445
 Ser Ile Thr Gly Ser Leu Gly Pro Leu Leu Asp Gly Thr Ala Thr Leu
 450 455 460
 Arg Leu Val Lys Arg Gln Val Pro Leu Asp Cys Val Leu Tyr Arg Tyr
 465 470 475 480
 Gly Ser Phe Ser Val Thr Leu Asp Ile Val Gln Gly Ile Glu Ser Ala
 485 490 495
 Glu Ile Leu Gln Ala Val Pro Ser Gly Glu Gly Asp Ala Phe Glu Leu
 500 505 510
 Thr Val Ser Cys Gln Gly Gly Leu Pro Lys Glu Ala Cys Met Glu Ile
 515 520 525
 Ser Ser Pro Gly Cys Gln Pro Pro Ala Gln Arg Leu Cys Gln Pro Val
 530 535 540
 Leu Pro Ser Pro Ala Cys Gln Leu Val Leu His Gln Ile Leu Lys Gly
 545 550 555 560
 Gly Ser Gly Thr Tyr Cys Leu Asn Val Ser Leu Ala Asp Thr Asn Ser
 565 570 575
 Leu Ala Val Val Ser Thr Gln Leu Ile Met Pro Gly Gln Glu Ala Gly
 580 585 590
 Leu Gly Gln Val Pro Leu Ile Val Gly Ile Leu Leu Val Leu Met Ala
 595 600 605
 Val Val Leu Ala Ser Leu Ile Tyr Arg Arg Arg Leu Met Lys Gln Asp
 610 615 620
 Phe Ser Val Pro Gln Leu Pro His Ser Ser Ser His Trp Leu Arg Leu
 625 630 635 640
 Pro Arg Ile Phe Cys Ser Cys Pro Ile Gly Glu Asn Ser Pro Leu Leu
 645 650 655
 Ser Gly Gln Gln Val
 660

<210> 71

<211> 309

<212> PRT

<213> Homo sapiens

<400> 71

Met Ser Leu Glu Gln Arg Ser Leu His Cys Lys Pro Glu Glu Ala Leu
 1 5 10 15
 Glu Ala Gln Gln Glu Ala Leu Gly Leu Val Cys Val Gln Ala Ala Thr
 20 25 30
 Ser Ser Ser Ser Pro Leu Val Leu Gly Thr Leu Glu Glu Val Pro Thr

```

      35              40              45
Ala Gly Ser Thr Asp Pro Pro Gln Ser Pro Gln Gly Ala Ser Ala Phe
  50              55              60
Pro Thr Thr Ile Asn Phe Thr Arg Gln Arg Gln Pro Ser Glu Gly Ser
  65              70              75              80
Ser Ser Arg Glu Glu Glu Gly Pro Ser Thr Ser Cys Ile Leu Glu Ser
      85              90              95
Leu Phe Arg Ala Val Ile Thr Lys Lys Val Ala Asp Leu Val Gly Phe
      100              105              110
Leu Leu Leu Lys Tyr Arg Ala Arg Glu Pro Val Thr Lys Ala Glu Met
      115              120              125
Leu Glu Ser Val Ile Lys Asn Tyr Lys His Cys Phe Pro Glu Ile Phe
      130              135              140
Gly Lys Ala Ser Glu Ser Leu Gln Leu Val Phe Gly Ile Asp Val Lys
      145              150              155              160
Glu Ala Asp Pro Thr Gly His Ser Tyr Val Leu Val Thr Cys Leu Gly
      165              170              175
Leu Ser Tyr Asp Gly Leu Leu Gly Asp Asn Gln Ile Met Pro Lys Thr
      180              185              190
Gly Phe Leu Ile Ile Val Leu Val Met Ile Ala Met Glu Gly Gly His
      195              200              205
Ala Pro Glu Glu Glu Ile Trp Glu Glu Leu Ser Val Met Glu Val Tyr
      210              215              220
Asp Gly Arg Glu His Ser Ala Tyr Gly Glu Pro Arg Lys Leu Leu Thr
      225              230              235              240
Gln Asp Leu Val Gln Glu Lys Tyr Leu Glu Tyr Arg Gln Val Pro Asp
      245              250              255
Ser Asp Pro Ala Arg Tyr Glu Phe Leu Trp Gly Pro Arg Ala Leu Ala
      260              265              270
Glu Thr Ser Tyr Val Lys Val Leu Glu Tyr Val Ile Lys Val Ser Ala
      275              280              285
Arg Val Arg Phe Phe Phe Pro Ser Leu Arg Glu Ala Ala Leu Arg Glu
      290              295              300
Glu Glu Glu Gly Val
      305

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<210> 72
 <211> 314
 <212> PRT
 <213> Homo sapiens

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<400> 72
Met Pro Leu Glu Gln Arg Ser Gln His Cys Lys Pro Glu Glu Gly Leu
  1              5              10              15
Glu Ala Arg Gly Glu Ala Leu Gly Leu Val Gly Ala Gln Ala Pro Ala
      20              25              30
Thr Glu Glu Gln Gln Thr Ala Ser Ser Ser Ser Thr Leu Val Glu Val
      35              40              45
Thr Leu Gly Glu Val Pro Ala Ala Asp Ser Pro Ser Pro Pro His Ser
      50              55              60
Pro Gln Gly Ala Ser Ser Phe Ser Thr Thr Ile Asn Tyr Thr Leu Trp
      65              70              75              80
Arg Gln Ser Asp Glu Gly Ser Ser Asn Gln Glu Glu Gly Pro Arg
      85              90              95
Met Phe Pro Asp Leu Glu Ser Glu Phe Gln Ala Ala Ile Ser Arg Lys
      100              105              110
Met Val Glu Leu Val His Phe Leu Leu Leu Lys Tyr Arg Ala Arg Glu
      115              120              125
Pro Val Thr Lys Ala Glu Met Leu Glu Ser Val Leu Arg Asn Cys Gln
      130              135              140

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Asp Phe Phe Pro Val Ile Phe Ser Lys Ala Ser Glu Tyr Leu Gln Leu
145          150          155          160
Val Phe Gly Ile Glu Val Val Glu Val Val Pro Ile Ser His Leu Tyr
          165          170          175
Ile Leu Val Thr Cys Leu Gly Leu Ser Tyr Asp Gly Leu Leu Gly Asp
          180          185          190
Asn Gln Val Met Pro Lys Thr Gly Leu Leu Ile Ile Val Leu Ala Ile
          195          200          205
Ile Ala Ile Glu Gly Asp Cys Ala Pro Glu Glu Lys Ile Trp Glu Glu
          210          215          220
Leu Ser Met Leu Glu Val Phe Glu Gly Arg Glu Asp Ser Val Phe Ala
225          230          235          240
His Pro Arg Lys Leu Leu Met Gln Asp Leu Val Gln Glu Asn Tyr Leu
          245          250          255
Glu Tyr Arg Gln Val Pro Gly Ser Asp Pro Ala Cys Tyr Glu Phe Leu
          260          265          270
Trp Gly Pro Arg Ala Leu Ile Glu Thr Ser Tyr Val Lys Val Leu His
          275          280          285
His Thr Leu Lys Ile Gly Gly Glu Pro His Ile Ser Tyr Pro Pro Leu
          290          295          300
His Glu Arg Ala Leu Arg Glu Gly Glu Glu
305          310

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<210> 73

<211> 314

<212> PRT

<213> Homo sapiens

<400> 73

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Met Pro Leu Glu Gln Arg Ser Gln His Cys Lys Pro Glu Glu Gly Leu
1      5      10      15
Glu Ala Arg Gly Glu Ala Leu Gly Leu Val Gly Ala Gln Ala Pro Ala
          20      25      30
Thr Glu Glu Gln Glu Ala Ala Ser Ser Ser Thr Leu Val Glu Val
          35      40      45
Thr Leu Gly Glu Val Pro Ala Ala Glu Ser Pro Asp Pro Pro Gln Ser
          50      55      60
Pro Gln Gly Ala Ser Ser Leu Pro Thr Thr Met Asn Tyr Pro Leu Trp
65          70      75          80
Ser Gln Ser Tyr Glu Asp Ser Ser Asn Gln Glu Glu Glu Gly Pro Ser
          85      90      95
Thr Phe Pro Asp Leu Glu Ser Glu Phe Gln Ala Ala Leu Ser Arg Lys
          100     105     110
Val Ala Glu Leu Val His Phe Leu Leu Lys Tyr Arg Ala Arg Glu
          115     120     125
Pro Val Thr Lys Ala Glu Met Leu Gly Ser Val Val Gly Asn Trp Gln
          130     135     140
Tyr Phe Phe Pro Val Ile Phe Ser Lys Ala Ser Ser Ser Leu Gln Leu
145          150          155          160
Val Phe Gly Ile Glu Leu Met Glu Val Asp Pro Ile Gly His Leu Tyr
          165          170          175
Ile Phe Ala Thr Cys Leu Gly Leu Ser Tyr Asp Gly Leu Leu Gly Asp
          180          185          190
Asn Gln Ile Met Pro Lys Ala Gly Leu Leu Ile Ile Val Leu Ala Ile
          195          200          205
Ile Ala Arg Glu Gly Asp Cys Ala Pro Glu Glu Lys Ile Trp Glu Glu
          210          215          220
Leu Ser Val Leu Glu Val Phe Glu Gly Arg Glu Asp Ser Ile Leu Gly
225          230          235          240
Asp Pro Lys Lys Leu Leu Thr Gln His Phe Val Gln Glu Asn Tyr Leu

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| | | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|--|
| | | | | 245 | | | | | 250 | | | | | 255 | | | |
| Glu | Tyr | Arg | Gln | Val | Pro | Gly | Ser | Asp | Pro | Ala | Cys | Tyr | Glu | Phe | Leu | | |
| | | | 260 | | | | | 265 | | | | | 270 | | | | |
| Trp | Gly | Pro | Arg | Ala | Leu | Val | Glu | Thr | Ser | Tyr | Val | Lys | Val | Leu | His | | |
| | | 275 | | | | | 280 | | | | | 285 | | | | | |
| His | Met | Val | Lys | Ile | Ser | Gly | Gly | Pro | His | Ile | Ser | Tyr | Pro | Pro | Leu | | |
| | 290 | | | | | 295 | | | | | 300 | | | | | | |
| His | Glu | Trp | Val | Leu | Arg | Glu | Gly | Glu | Glu | | | | | | | | |
| 305 | | | | | 310 | | | | | | | | | | | | |

<210> 74

<211> 180

<212> PRT

<213> Homo sapiens

<400> 74

| | | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|--|
| Met | Gln | Ala | Glu | Gly | Arg | Gly | Thr | Gly | Gly | Ser | Thr | Gly | Asp | Ala | Asp | | |
| 1 | | | | 5 | | | | 10 | | | | | 15 | | | | |
| Gly | Pro | Gly | Gly | Pro | Gly | Ile | Pro | Asp | Gly | Pro | Gly | Gly | Asn | Ala | Gly | | |
| | | 20 | | | | | | 25 | | | | 30 | | | | | |
| Gly | Pro | Gly | Glu | Ala | Gly | Ala | Thr | Gly | Gly | Arg | Gly | Pro | Arg | Gly | Ala | | |
| | 35 | | | | | 40 | | | | | 45 | | | | | | |
| Gly | Ala | Ala | Arg | Ala | Ser | Gly | Pro | Gly | Gly | Gly | Ala | Pro | Arg | Gly | Pro | | |
| | 50 | | | | 55 | | | | | 60 | | | | | | | |
| His | Gly | Gly | Ala | Ala | Ser | Gly | Leu | Asn | Gly | Cys | Cys | Arg | Cys | Gly | Ala | | |
| 65 | | | | | 70 | | | 75 | | | | | | 80 | | | |
| Arg | Gly | Pro | Glu | Ser | Arg | Leu | Leu | Glu | Phe | Tyr | Leu | Ala | Met | Pro | Phe | | |
| | | | 85 | | | | | 90 | | | | | 95 | | | | |
| Ala | Thr | Pro | Met | Glu | Ala | Glu | Leu | Ala | Arg | Arg | Ser | Leu | Ala | Gln | Asp | | |
| | | 100 | | | | | | 105 | | | | | 110 | | | | |
| Ala | Pro | Pro | Leu | Pro | Val | Pro | Gly | Val | Leu | Leu | Lys | Glu | Phe | Thr | Val | | |
| | | 115 | | | | | 120 | | | | | 125 | | | | | |
| Ser | Gly | Asn | Ile | Leu | Thr | Ile | Arg | Leu | Thr | Ala | Ala | Asp | His | Arg | Gln | | |
| | 130 | | | | | 135 | | | | | 140 | | | | | | |
| Leu | Gln | Leu | Ser | Ile | Ser | Ser | Cys | Leu | Gln | Gln | Leu | Ser | Leu | Leu | Met | | |
| 145 | | | | | 150 | | | | 155 | | | | | | 160 | | |
| Trp | Ile | Thr | Gln | Cys | Phe | Leu | Pro | Val | Phe | Leu | Ala | Gln | Pro | Pro | Ser | | |
| | | | 165 | | | | | 170 | | | | | | 175 | | | |
| Gly | Gln | Arg | Arg | | | | | | | | | | | | | | |
| | | | 180 | | | | | | | | | | | | | | |

<210> 75

<211> 180

<212> PRT

<213> Homo sapiens

<400> 75

| | | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|--|
| Met | Gln | Ala | Glu | Gly | Arg | Gly | Thr | Gly | Gly | Ser | Thr | Gly | Asp | Ala | Asp | | |
| 1 | | | | 5 | | | | 10 | | | | | 15 | | | | |
| Gly | Pro | Gly | Gly | Pro | Gly | Ile | Pro | Asp | Gly | Pro | Gly | Gly | Asn | Ala | Gly | | |
| | | 20 | | | | | | 25 | | | | 30 | | | | | |
| Gly | Pro | Gly | Glu | Ala | Gly | Ala | Thr | Gly | Gly | Arg | Gly | Pro | Arg | Gly | Ala | | |
| | 35 | | | | | 40 | | | | | 45 | | | | | | |
| Gly | Ala | Ala | Arg | Ala | Ser | Gly | Pro | Arg | Gly | Gly | Ala | Pro | Arg | Gly | Pro | | |
| | 50 | | | | 55 | | | | | 60 | | | | | | | |
| His | Gly | Gly | Ala | Ala | Ser | Ala | Gln | Asp | Gly | Arg | Cys | Pro | Cys | Gly | Ala | | |
| 65 | | | | | 70 | | | 75 | | | | | | 80 | | | |
| Arg | Arg | Pro | Asp | Ser | Arg | Leu | Leu | Glu | Leu | His | Ile | Thr | Met | Pro | Phe | | |
| | | | | 85 | | | | 90 | | | | | 95 | | | | |

Ser Ser Pro Met Glu Ala Glu Leu Val Arg Arg Ile Leu Ser Arg Asp
 100 105 110
 Ala Ala Pro Leu Pro Arg Pro Gly Ala Val Leu Lys Asp Phe Thr Val
 115 120 125
 Ser Gly Asn Leu Leu Phe Ile Arg Leu Thr Ala Ala Asp His Arg Gln
 130 135 140
 Leu Gln Leu Ser Ile Ser Ser Cys Leu Gln Gln Leu Ser Leu Leu Met
 145 150 155 160
 Trp Ile Thr Gln Cys Phe Leu Pro Val Phe Leu Ala Gln Ala Pro Ser
 165 170 175
 Gly Gln Arg Arg
 180

<210> 76
 <211> 210
 <212> PRT
 <213> Homo sapiens

<400> 76
 Met Gln Ala Glu Gly Arg Gly Thr Gly Gly Ser Thr Gly Asp Ala Asp
 1 5 10 15
 Gly Pro Gly Gly Pro Gly Ile Pro Asp Gly Pro Gly Gly Asn Ala Gly
 20 25 30
 Gly Pro Gly Glu Ala Gly Ala Thr Gly Gly Arg Gly Pro Arg Gly Ala
 35 40 45
 Gly Ala Ala Arg Ala Ser Gly Pro Arg Gly Gly Ala Pro Arg Gly Pro
 50 55 60
 His Gly Gly Ala Ala Ser Ala Gln Asp Gly Arg Cys Pro Cys Gly Ala
 65 70 75 80
 Arg Arg Pro Asp Ser Arg Leu Leu Glu Leu His Ile Thr Met Pro Phe
 85 90 95
 Ser Ser Pro Met Glu Ala Glu Leu Val Arg Arg Ile Leu Ser Arg Asp
 100 105 110
 Ala Ala Pro Leu Pro Arg Pro Gly Ala Val Leu Lys Asp Phe Thr Val
 115 120 125
 Ser Gly Asn Leu Leu Phe Met Ser Val Trp Asp Gln Asp Arg Glu Gly
 130 135 140
 Ala Gly Arg Met Arg Val Val Gly Trp Gly Leu Gly Ser Ala Ser Pro
 145 150 155 160
 Glu Gly Gln Lys Ala Arg Asp Leu Arg Thr Pro Lys His Lys Val Ser
 165 170 175
 Glu Gln Arg Pro Gly Thr Pro Gly Pro Pro Pro Pro Glu Gly Ala Gln
 180 185 190
 Gly Asp Gly Cys Arg Gly Val Ala Phe Asn Val Met Phe Ser Ala Pro
 195 200 205
 His Ile
 210

<210> 77
 <211> 509
 <212> PRT
 <213> Homo sapiens

<400> 77
 Met Glu Arg Arg Arg Leu Trp Gly Ser Ile Gln Ser Arg Tyr Ile Ser
 1 5 10 15
 Met Ser Val Trp Thr Ser Pro Arg Arg Leu Val Glu Leu Ala Gly Gln
 20 25 30
 Ser Leu Leu Lys Asp Glu Ala Leu Ala Ile Ala Ala Leu Glu Leu Leu

| | | |
|---------------------|-------------------------|---------------------|
| 35 | 40 | 45 |
| Pro Arg Glu Leu Phe | Pro Pro Leu Phe Met Ala | Ala Phe Asp Gly Arg |
| 50 | 55 | 60 |
| His Ser Gln Thr Leu | Lys Ala Met Val Gln Ala | Trp Pro Phe Thr Cys |
| 65 | 70 | 75 |
| Leu Pro Leu Gly Val | Leu Met Lys Gly Gln His | Leu His Leu Glu Thr |
| 85 | 90 | 95 |
| Phe Lys Ala Val Leu | Asp Gly Leu Asp Val Leu | Leu Ala Gln Glu Val |
| 100 | 105 | 110 |
| Arg Pro Arg Arg Trp | Lys Leu Gln Val Leu Asp | Leu Arg Lys Asn Ser |
| 115 | 120 | 125 |
| His Gln Asp Phe Trp | Thr Val Trp Ser Gly Asn | Arg Ala Ser Leu Tyr |
| 130 | 135 | 140 |
| Ser Phe Pro Glu Pro | Glu Ala Ala Gln Pro Met | Thr Lys Lys Arg Lys |
| 145 | 150 | 155 |
| Val Asp Gly Leu Ser | Thr Glu Ala Glu Gln Pro | Phe Ile Pro Val Glu |
| 165 | 170 | 175 |
| Val Leu Val Asp Leu | Phe Leu Lys Glu Gly Ala | Cys Asp Glu Leu Phe |
| 180 | 185 | 190 |
| Ser Tyr Leu Ile Glu | Lys Val Lys Arg Lys Lys | Asn Val Leu Arg Leu |
| 195 | 200 | 205 |
| Cys Cys Lys Lys Leu | Lys Ile Phe Ala Met Pro | Met Gln Asp Ile Lys |
| 210 | 215 | 220 |
| Met Ile Leu Lys Met | Val Gln Leu Asp Ser Ile | Glu Asp Leu Glu Val |
| 225 | 230 | 235 |
| Thr Cys Thr Trp Lys | Leu Pro Thr Leu Ala Lys | Phe Ser Pro Tyr Leu |
| 245 | 250 | 255 |
| Gly Gln Met Ile Asn | Leu Arg Arg Leu Leu Ser | His Ile His Ala |
| 260 | 265 | 270 |
| Ser Ser Tyr Ile Ser | Pro Glu Lys Glu Glu Gln | Tyr Ile Ala Gln Phe |
| 275 | 280 | 285 |
| Thr Ser Gln Phe Leu | Ser Leu Gln Cys Leu Gln | Ala Leu Tyr Val Asp |
| 290 | 295 | 300 |
| Ser Leu Phe Phe Leu | Arg Gly Arg Leu Asp Gln | Leu Leu Arg His Val |
| 305 | 310 | 315 |
| Met Asn Pro Leu Glu | Thr Leu Ser Ile Thr Asn | Cys Arg Leu Ser Glu |
| 325 | 330 | 335 |
| Gly Asp Val Met His | Leu Ser Gln Ser Pro Ser | Val Ser Gln Leu Ser |
| 340 | 345 | 350 |
| Val Leu Ser Leu Ser | Gly Val Met Leu Thr Asp | Val Ser Pro Glu Pro |
| 355 | 360 | 365 |
| Leu Gln Ala Leu Leu | Glu Arg Ala Ser Ala Thr | Leu Gln Asp Leu Val |
| 370 | 375 | 380 |
| Phe Asp Glu Cys Gly | Ile Thr Asp Asp Gln Leu | Ala Leu Leu Pro |
| 385 | 390 | 395 |
| Ser Leu Ser His Cys | Ser Gln Leu Thr Thr Leu | Ser Phe Tyr Gly Asn |
| 405 | 410 | 415 |
| Ser Ile Ser Ile Ser | Ala Leu Gln Ser Leu Leu | Gln His Leu Ile Gly |
| 420 | 425 | 430 |
| Leu Ser Asn Leu Thr | His Val Leu Tyr Pro Val | Pro Leu Glu Ser Tyr |
| 435 | 440 | 445 |
| Glu Asp Ile His Gly | Thr Leu His Leu Glu Arg | Leu Ala Tyr Leu His |
| 450 | 455 | 460 |
| Ala Arg Leu Arg Glu | Leu Leu Cys Glu Leu Gly | Arg Pro Ser Met Val |
| 465 | 470 | 475 |
| Trp Leu Ser Ala Asn | Pro Cys Pro His Cys Gly | Asp Arg Thr Phe Tyr |
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 <212> PRT
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 Phe His Pro Glu Asp Thr Gly Gln Val Phe Gln Val Ser His Ser Phe
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 <213> Homo sapiens

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 Gly Cys Ser Leu Asn Cys Val Asp Asp Ser Gln Asp Tyr Tyr Val Gly
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 Lys Lys Asn Ile Thr Cys Cys Asp Thr Asp Leu Cys Asn Ala Ser Gly
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<212> DNA
<213> Homo sapiens

<400> 81

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<212> DNA
<213> Homo sapiens

<400> 82

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<213> Homo sapiens

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| accccgccga | cccccgccgc | tttagccacg | gggaactctg | gggacagagc | ttaatgtggc | 660 |
| cagggcaggg | ctggttagaa | gaggtcaggg | cccacgctgt | ggcaggaatc | aaggtcagga | 720 |
| ccccgagagg | gaactgaggg | cagcctaacc | accaccctca | ccaccattcc | cgtcccccaa | 780 |
| cacccaaccc | cacccccatc | ccccattccc | atccccaccc | ccaccctat | cctggcagaa | 840 |
| tcggggcttt | gcccctggta | tcaagtccag | gaagctccgg | gaatggcggc | caggcacgtg | 900 |
| agtccctgag | ttcacatcta | cggctaaggg | agggaaaggg | ttcgggtatc | cgagtatggc | 960 |
| cgctggggag | cagcgaaggg | gcccaggcct | cctggaagac | agtggagtcc | tgaggggacc | 1020 |
| cagcatgcca | ggacaggggg | cccactgtac | ccctgtctca | aaccgaggca | ccttttccatt | 1080 |
| cggctacggg | aatcctaggg | atgcagaccc | acttcagcag | ggggttgggg | cccagccctg | 1140 |
| cgaggagtca | tggggaggaa | gaagagggag | gactgagggg | accttggagt | ccagatcagt | 1200 |
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| ccttcagggt | gaccagagag | ttgagggctg | tggtctgaag | agtgggactt | caggtcagca | 1320 |
| gagggaggaa | tcccaggatc | tgccagggcc | aaggtgtacc | ccaagggggc | ccctatgtgg | 1380 |
| tggacagatg | cagtgtctct | aggatctgcc | aagcatccag | gtgaagagac | tgagggagga | 1440 |
| ttgaggttac | ccctgggaca | gaatgoggac | tgggggccccc | ataaaaaatc | gccctgctcc | 1500 |
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| atcactgatg | tcaggggaag | ggaagccttg | gtctgagggg | gctgcactca | gggcagtaga | 1620 |
| gggaggctct | cagaccctac | taggagtggg | ggtgaggacc | aagcagctct | ctcaccacag | 1680 |
| gtacatggac | ttcaataaat | ttggacatct | ctcgttgtcc | tttccgggag | gacctgggaa | 1740 |
| tgtatggcca | gatgtgggtc | ccctcatgtt | tttctgtacc | atatcaggta | tgtgagttct | 1800 |
| tgacatgaga | gattctcagg | ccagcagaag | ggagggatta | ggccctataa | ggagaaaggt | 1860 |
| gagggccctg | agtgagcaca | gaggggatcc | tccaccccag | tagagtgggg | acctcacaga | 1920 |
| gtctggccaa | ccctcctgac | agttctggga | atccgtggct | gcgtttgctg | tctgcacatt | 1980 |
| gggggcccgt | ggattcctct | cccaggaatc | aggagctcca | ggaacaaggc | agtgaggact | 2040 |
| tggctctgag | cagtgtcctc | aggtcacaga | gtagaggggg | ctcagatagt | gccaacgggtg | 2100 |
| aaggtttgcc | ttggattcaa | accaagggcc | ccacctgccc | cagaacacat | ggactccaga | 2160 |
| gcgcctggcc | tcaccctcaa | tactttcagt | cctgcagcct | cagcatgcgc | tggccgggatg | 2220 |
| taccctgagg | tgccctctca | cttcctcctt | caggttctga | ggggacaggc | tgacctggag | 2280 |
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| cctccaaggt | tccattcagt | actcagctga | ggtctctcac | atgctccctc | tctccccagg | 2400 |
| ccagtgggtc | tccattgccc | agctcctgcc | cacactcccg | cctgttgccc | tgaccagagt | 2460 |
| catcatgcct | cttgagcaga | ggagtacgca | ctgcaagcct | gaagaaggcc | ttgaggcccg | 2520 |
| aggagaggcc | ctgggcctgg | tgggtgcgca | ggctcctgct | actgaggagc | aggaggctgc | 2580 |
| ctcctcctct | tctactctag | ttgaagtcac | cctggggggg | gtgcctgctg | ccgagtcacc | 2640 |
| agatcctccc | cagagtccct | agggagcctc | cagcctcccc | actaccatga | actaccctct | 2700 |
| ctggagccaa | tcctatgagg | actccagcaa | ccaagaagag | gaggggccaa | gcaccttccc | 2760 |
| tgacctggag | tccgagttcc | aagcagcact | cagtaggaag | gtggccgagt | tgggttcattt | 2820 |
| tctgtcctcc | aagtatcgag | ccaggggagcc | ggtcacaaag | gcagaaatgc | tggggagtg | 2880 |

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gctgtagagc ctaggacctg cagtcataata attaggtgg tgagaagtcc tghtaagatgt 4140
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gtgc 4204

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<210> 84
 <211> 752
 <212> DNA
 <213> Homo sapiens

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<400> 84
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ttcctgatgg ccaggggggc aatgctggcg gccagggaga ggcgggtgcc acgggcggca 180
gaggtccccg ggcgcgaggg gcagcaaggg cctcggggcc gggaggaggc gcccgcgggg 240
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cggagagccg cctgcttagg ttctacctcg ccctgccttt cgcgacaccc atggaagcag 360
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cgcagtgtct tctgcccgtg tttttggctc agcctccctc agggcagagg cgctaagccc 600
agcctggcgc cccttccctag gtcattgcctc ctcccctagg gaatgggtccc agcacgagtg 660
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<210> 85
 <211> 2148
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
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 <223> n = A,T,C or G

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acgaaggcgt ttgtgggggt ccattcagag ccgatacatc agcatgagtg tgtggacaag 300
cccacggaga cttgtggagc tggcagggca gagcctgctg aaggatgagg ccctggccat 360

```

| | | | | | | |
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| tgccgccctg | gagttgctgc | ccagggagct | cttcccccca | ctcttcatgg | cagcccttga | 420 |
| cgggagacac | agccagaccc | tgaaggcaat | ggtgcaggcc | tggcccttca | cctgcctccc | 480 |
| tctgggagtg | ctgatgaagg | gacaacatct | tcacctggag | accttcaaag | ctgtgcttga | 540 |
| tggacttgat | gtgctccttg | cccaggaggt | tgcgccagg | aggtggaaac | ttcaagtgtc | 600 |
| ggatttacgg | aagaactctc | atcaggactt | ctggactgta | tggctctggaa | acagggccag | 660 |
| tctgtactca | tttccagagc | cagaagcagc | tcagcccatg | acaaagaagc | gaaaagtaga | 720 |
| tggtttgagc | acagaggcag | agcagccctt | cattccagta | gaggtgctcg | tagacctgtt | 780 |
| cctcaaggaa | ggtgcctgtg | atgaattgtt | ctcctacctc | attgagaaaag | tgaagcgaaa | 840 |
| gaaaaatgta | ctacgcctgt | gctgtaagaa | gctgaagatt | tttgcaatgc | ccatgcagga | 900 |
| tatcaagatg | atcctgaaaa | tgggtgcagct | ggactctatt | gaagatttgg | aagtgaactg | 960 |
| tacctggaag | ctacccacct | tggcgaaatt | ttctccttac | ctggggccaga | tgattaatct | 1020 |
| gcgtagactc | ctcctctccc | acatccatgc | atcttctctac | atttccccgg | agaaggaaga | 1080 |
| gcagtatatc | gcccagttca | cctctcagtt | cctcagtcctg | cagtgcctgc | aggctctcta | 1140 |
| tgtggactct | ttattttttcc | ttagaggccg | cctggatcag | ttgctcaggc | acgtgatgaa | 1200 |
| ccccttgga | accctctcaa | taactaactg | cggcctttcg | gaaggggatg | tgatgcatct | 1260 |
| gtcccagagt | cccagcgtca | gtcagctaag | tgtcctgagt | ctaagtgggg | tcatgctgac | 1320 |
| cgatgtaagt | cccagagccc | tccaagctct | gctggagaga | gcctctgcca | ccctccagga | 1380 |
| cctggctctt | gatgagtgtg | ggatcacgga | tgatcagctc | cttgccctcc | tgccctccct | 1440 |
| gagccactgc | tcccagctta | caaccttaag | cttctacggg | aattccatct | ccatactctg | 1500 |
| cttgacagtg | ctcctgcagc | acctcatcgg | gctgagcaat | ctgacccacg | tgctgtatcc | 1560 |
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| tctgcatgcc | aggctcaggg | agttgtctgtg | tgagttgggg | cggcccagca | tggctctggct | 1680 |
| tagtgccaac | ccctgtcctc | actgtgggga | cagaaccttc | tatgaccogg | agcccatcct | 1740 |
| gtgcccctgt | ttcatgccta | actagctggg | tgcacatatc | aaatgcttca | ttctgcatac | 1800 |
| ttggacacta | aagccaggat | gtgcatgcat | cttgaagcaa | caaagcagcc | acagtttcag | 1860 |
| acaaatgttc | agtgtgagtg | aggaaaacat | gttcagtgag | gaaaaaacat | tcagacaaat | 1920 |
| gttcagtgag | gaaaaaaaag | ggaagtgtgg | gataggcaga | tgttgacttg | aggagttaat | 1980 |
| gtgatctttg | gggagataca | tcttatagag | ttagaatatg | aatctgaatt | tctaaaggga | 2040 |
| gattctggct | tgggaagtac | atgtaggagt | taatccctgt | gtagactgtt | gtaaagaaac | 2100 |
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<210> 86

<211> 1466

<212> DNA

<213> Homo sapiens

<400> 86

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| cttctctcacc | ctgtccgtga | cgtggattgg | tgtctgcacc | ctcatcctgt | ctcggattgt | 120 |
| gggaggctgg | gagtgcgaga | agcattccca | accctggcag | gtgcttgtgg | cctctcgtgg | 180 |
| cagggcagtc | tgcggcggtg | ttctggtgca | ccccagtg | gtcctcacag | ctgcccactg | 240 |
| catcaggaac | aaaagcgtga | tcttgctggg | tgggcacagc | ctgtttcatc | ctgaagacac | 300 |
| aggccaggta | tttcagggtca | gccacagctt | cccacacccg | ctctacgata | tgagcctcct | 360 |
| gaagaatcga | ttcctcaggc | caggtgatga | ctccagccac | gacctcatgc | tgctccgcct | 420 |
| gtcagagcct | gccgagctca | cggatgctgt | gaaggtcatg | gacctgccc | cccaggagcc | 480 |
| agcactgggg | accacctgct | acgcctcagg | ctggggcagc | attgaaccag | aggagtctct | 540 |
| gaccccaaag | aaacttcagt | gtgtggacct | ccatgttatt | tccaatgacg | tgtgtgcgca | 600 |
| agttcacccct | cagaagggtga | ccaagttcat | gctgtgtgtc | ggacgctgga | cagggggcaa | 660 |
| aagcacctgc | tcgggtgatt | ctgggggccc | acttgtctgt | aatgggtgtg | ttcaagggtat | 720 |
| cacgtcatgg | ggcagtgaac | catgtgccct | gcccgaagag | ccttccctgt | acaccaagg | 780 |
| ggtgcattac | cggaagtgg | tcaaggacac | catcgtggcc | aacccttgag | cacccctatc | 840 |
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| ctgggggaata | ctggccatgc | ctggagacat | atcactcaat | ttctctgagg | acacagatag | 1080 |
| gatgggggtg | ctgtgtttatt | tgtgggggtac | agagatgaaa | gaggggtggg | atccacactg | 1140 |
| agagagtgg | gagtgcacatg | tgtctggacac | tgtccatgaa | gcactgagca | gaagctggag | 1200 |
| gcacaacgca | ccagacactc | acagcaagga | tggagctgaa | aacataaccc | actctgtcct | 1260 |
| ggaggcactg | ggaagcctag | agaaggctgt | gagccaagga | gggagggtct | tcctttggca | 1320 |
| tgggatgggg | atgaagtaag | gagagggact | ggacccctg | gaagctgatt | cactatgggg | 1380 |
| ggaggtgtat | tgaagtcctc | cagacaaccc | tcagatttga | tgatttccta | gtagaactca | 1440 |

cagaaataaa gagctgttat actgtg

1466

<210> 87

<211> 990

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(990)

<223> n = A,T,C or G

<400> 87

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<210> 88

<211> 702

<212> PRT

<213> Homo sapiens

<400> 88

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      20           25           30
Thr Ala Lys Leu Thr Ile Glu Ser Thr Pro Phe Asn Val Ala Glu Gly
      35           40           45
Lys Glu Val Leu Leu Leu Val His Asn Leu Pro Gln His Leu Phe Gly
      50           55           60
Tyr Ser Trp Tyr Lys Gly Glu Arg Val Asp Gly Asn Arg Gln Ile Ile
      65           70           75           80
Gly Tyr Val Ile Gly Thr Gln Gln Ala Thr Pro Gly Pro Ala Tyr Ser
      85           90           95
Gly Arg Glu Ile Ile Tyr Pro Asn Ala Ser Leu Leu Ile Gln Asn Ile
      100          105          110
Ile Gln Asn Asp Thr Gly Phe Tyr Thr Leu His Val Ile Lys Ser Asp
      115          120          125
Leu Val Asn Glu Glu Ala Thr Gly Gln Phe Arg Val Tyr Pro Glu Leu
      130          135          140
Pro Lys Pro Ser Ile Ser Ser Asn Asn Ser Lys Pro Val Glu Asp Lys
      145          150          155          160
Asp Ala Val Ala Phe Thr Cys Glu Pro Glu Thr Gln Asp Ala Thr Tyr
      165          170          175
Leu Trp Trp Val Asn Asn Gln Ser Leu Pro Val Ser Pro Arg Leu Gln
      180          185          190

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| | | | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Leu | Ser | Asn | Gly | Asn | Arg | Thr | Leu | Thr | Leu | Phe | Asn | Val | Thr | Arg | Asn | 195 | 200 | 205 |
| Asp | Thr | Ala | Ser | Tyr | Lys | Cys | Glu | Thr | Gln | Asn | Pro | Val | Ser | Ala | Arg | 210 | 215 | 220 |
| Arg | Ser | Asp | Ser | Val | Ile | Leu | Asn | Val | Leu | Tyr | Gly | Pro | Asp | Ala | Pro | 225 | 230 | 235 |
| Thr | Ile | Ser | Pro | Leu | Asn | Thr | Ser | Tyr | Arg | Ser | Gly | Glu | Asn | Leu | Asn | 245 | 250 | 255 |
| Leu | Ser | Cys | His | Ala | Ala | Ser | Asn | Pro | Pro | Ala | Gln | Tyr | Ser | Trp | Phe | 260 | 265 | 270 |
| Val | Asn | Gly | Thr | Phe | Gln | Gln | Ser | Thr | Gln | Glu | Leu | Phe | Ile | Pro | Asn | 275 | 280 | 285 |
| Ile | Thr | Val | Asn | Asn | Ser | Gly | Ser | Tyr | Thr | Cys | Gln | Ala | His | Asn | Ser | 290 | 295 | 300 |
| Asp | Thr | Gly | Leu | Asn | Arg | Thr | Thr | Val | Thr | Thr | Ile | Thr | Val | Tyr | Ala | 305 | 310 | 315 |
| Glu | Pro | Pro | Lys | Pro | Phe | Ile | Thr | Ser | Asn | Asn | Ser | Asn | Pro | Val | Glu | 325 | 330 | 335 |
| Asp | Glu | Asp | Ala | Val | Ala | Leu | Thr | Cys | Glu | Pro | Glu | Ile | Gln | Asn | Thr | 340 | 345 | 350 |
| Thr | Tyr | Leu | Trp | Trp | Val | Asn | Asn | Gln | Ser | Leu | Pro | Val | Ser | Pro | Arg | 355 | 360 | 365 |
| Leu | Gln | Leu | Ser | Asn | Asp | Asn | Arg | Thr | Leu | Thr | Leu | Leu | Ser | Val | Thr | 370 | 375 | 380 |
| Arg | Asn | Asp | Val | Gly | Pro | Tyr | Glu | Cys | Gly | Ile | Gln | Asn | Glu | Leu | Ser | 385 | 390 | 395 |
| Val | Asp | His | Ser | Asp | Pro | Val | Ile | Leu | Asn | Val | Leu | Tyr | Gly | Pro | Asp | 405 | 410 | 415 |
| Asp | Pro | Thr | Ile | Ser | Pro | Ser | Tyr | Thr | Tyr | Tyr | Arg | Pro | Gly | Val | Asn | 420 | 425 | 430 |
| Leu | Ser | Leu | Ser | Cys | His | Ala | Ala | Ser | Asn | Pro | Pro | Ala | Gln | Tyr | Ser | 435 | 440 | 445 |
| Trp | Leu | Ile | Asp | Gly | Asn | Ile | Gln | Gln | His | Thr | Gln | Glu | Leu | Phe | Ile | 450 | 455 | 460 |
| Ser | Asn | Ile | Thr | Glu | Lys | Asn | Ser | Gly | Leu | Tyr | Thr | Cys | Gln | Ala | Asn | 465 | 470 | 475 |
| Asn | Ser | Ala | Ser | Gly | His | Ser | Arg | Thr | Thr | Val | Lys | Thr | Ile | Thr | Val | 485 | 490 | 495 |
| Ser | Ala | Glu | Leu | Pro | Lys | Pro | Ser | Ile | Ser | Ser | Asn | Asn | Ser | Lys | Pro | 500 | 505 | 510 |
| Val | Glu | Asp | Lys | Asp | Ala | Val | Ala | Phe | Thr | Cys | Glu | Pro | Glu | Ala | Gln | 515 | 520 | 525 |
| Asn | Thr | Thr | Tyr | Leu | Trp | Trp | Val | Asn | Gly | Gln | Ser | Leu | Pro | Val | Ser | 530 | 535 | 540 |
| Pro | Arg | Leu | Gln | Leu | Ser | Asn | Gly | Asn | Arg | Thr | Leu | Thr | Leu | Phe | Asn | 545 | 550 | 555 |
| Val | Thr | Arg | Asn | Asp | Ala | Arg | Ala | Tyr | Val | Cys | Gly | Ile | Gln | Asn | Ser | 565 | 570 | 575 |
| Val | Ser | Ala | Asn | Arg | Ser | Asp | Pro | Val | Thr | Leu | Asp | Val | Leu | Tyr | Gly | 580 | 585 | 590 |
| Pro | Asp | Thr | Pro | Ile | Ile | Ser | Pro | Pro | Asp | Ser | Ser | Tyr | Leu | Ser | Gly | 595 | 600 | 605 |
| Ala | Asn | Leu | Asn | Leu | Ser | Cys | His | Ser | Ala | Ser | Asn | Pro | Ser | Pro | Gln | 610 | 615 | 620 |
| Tyr | Ser | Trp | Arg | Ile | Asn | Gly | Ile | Pro | Gln | Gln | His | Thr | Gln | Val | Leu | 625 | 630 | 635 |
| Phe | Ile | Ala | Lys | Ile | Thr | Pro | Asn | Asn | Asn | Gly | Thr | Tyr | Ala | Cys | Phe | 645 | 650 | 655 |
| Val | Ser | Asn | Leu | Ala | Thr | Gly | Arg | Asn | Asn | Ser | Ile | Val | Lys | Ser | Ile | 660 | 665 | 670 |
| Thr | Val | Ser | Ala | Ser | Gly | Thr | Ser | Pro | Gly | Leu | Ser | Ala | Gly | Ala | Thr | | | |

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 Trp Glu Leu Met Thr Phe Gly Ala Lys Pro Tyr Asp Gly Ile Pro Ala

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| 930 | 935 | 940 |
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| 945 | 950 | 955 |
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| 965 | 970 | 975 |
| Ser Arg Met Ala Arg Asp | Pro Gln Arg Phe Val | Val Ile Gln Asn Glu |
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          35          40          45
Pro Phe Ala Lys Thr Asn Leu Ser Lys Asn Gly Glu Asn Ile Asp Ser
          50          55          60
Asp Pro Ala Leu Gln Lys Val Asn Phe Leu Pro Val Leu Glu Gln Val
65          70          75          80
Gly Asn Ser Asp Cys His Tyr Gln Glu Gly Leu Lys Asp Ser Asp Leu
          85          90          95
Glu Asn Ser Glu Gly Leu Ser Arg Val Phe Ser Lys Leu Tyr Lys Glu
          100          105          110
Ala Glu Lys Ile Lys Lys Trp Lys Val Ser Thr Glu Ala Glu Leu Arg
          115          120          125
Gln Lys Glu Ser Lys Leu Gln Glu Asn Arg Lys Ile Ile Glu Ala Gln
          130          135          140
Arg Lys Ala Ile Gln Glu Leu Gln Phe Gly Asn Glu Lys Val Ser Leu
145          150          155          160
Lys Leu Glu Glu Gly Ile Gln Glu Asn Lys Asp Leu Ile Lys Glu Asn
          165          170          175
Asn Ala Thr Arg His Leu Cys Asn Leu Leu Lys Glu Thr Cys Ala Arg
          180          185          190
Ser Ala Glu Lys Thr Lys Lys Tyr Glu Tyr Glu Arg Glu Glu Thr Arg
          195          200          205
Gln Val Tyr Met Asp Leu Asn Asn Asn Ile Glu Lys Met Ile Thr Ala
          210          215          220
His Gly Glu Leu Arg Val Gln Ala Glu Asn Ser Arg Leu Glu Met His
225          230          235          240
Phe Lys Leu Lys Glu Asp Tyr Glu Lys Ile Gln His Leu Glu Gln Glu
          245          250          255
Tyr Lys Lys Glu Ile Asn Asp Lys Glu Lys Gln Val Ser Leu Leu Leu
          260          265          270
Ile Gln Ile Thr Glu Lys Glu Asn Lys Met Lys Asp Leu Thr Phe Leu
          275          280          285
Leu Glu Glu Ser Arg Asp Lys Val Asn Gln Leu Glu Glu Lys Thr Lys
          290          295          300
Leu Gln Ser Glu Asn Leu Lys Gln Ser Ile Glu Lys Gln His His Leu
305          310          315          320
Thr Lys Glu Leu Glu Asp Ile Lys Val Ser Leu Gln Arg Ser Val Ser
          325          330          335
Thr Gln Lys Ala Leu Glu Glu Asp Leu Gln Ile Ala Thr Lys Thr Ile
          340          345          350
Cys Gln Leu Thr Glu Glu Lys Glu Thr Gln Met Glu Glu Ser Asn Lys
          355          360          365
Ala Arg Ala Ala His Ser Phe Val Val Thr Glu Phe Glu Thr Thr Val
          370          375          380
Cys Ser Leu Glu Glu Leu Leu Arg Thr Glu Gln Gln Arg Leu Glu Lys

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| | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|---------|
| 385 | | | | | 390 | | | | | 395 | | | | 400 |
| Asn | Glu | Asp | Gln | Leu | Lys | Ile | Leu | Thr | Met | Glu | Leu | Gln | Lys | Lys Ser |
| | | | | 405 | | | | | 410 | | | | | 415 |
| Ser | Glu | Leu | Glu | Glu | Met | Thr | Lys | Leu | Thr | Asn | Asn | Lys | Glu | Val Glu |
| | | | 420 | | | | | 425 | | | | | 430 | |
| Leu | Glu | Glu | Leu | Lys | Lys | Val | Leu | Gly | Glu | Lys | Glu | Thr | Leu | Leu Tyr |
| | | | 435 | | | | 440 | | | | | 445 | | |
| Glu | Asn | Lys | Gln | Phe | Glu | Lys | Ile | Ala | Glu | Glu | Leu | Lys | Gly | Thr Glu |
| | 450 | | | | | 455 | | | | 460 | | | | |
| Gln | Glu | Leu | Ile | Gly | Leu | Leu | Gln | Ala | Arg | Glu | Lys | Glu | Val | His Asp |
| 465 | | | | | 470 | | | | | 475 | | | | 480 |
| Leu | Glu | Ile | Gln | Leu | Thr | Ala | Ile | Thr | Thr | Ser | Glu | Gln | Tyr | Tyr Ser |
| | | | 485 | | | | | 490 | | | | | | 495 |
| Lys | Glu | Val | Lys | Asp | Leu | Lys | Thr | Glu | Leu | Glu | Asn | Glu | Lys | Leu Lys |
| | | | 500 | | | | | 505 | | | | 510 | | |
| Asn | Thr | Glu | Leu | Thr | Ser | His | Cys | Asn | Lys | Leu | Ser | Leu | Glu | Asn Lys |
| | 515 | | | | | | 520 | | | | | 525 | | |
| Glu | Leu | Thr | Gln | Glu | Thr | Ser | Asp | Met | Thr | Leu | Glu | Leu | Lys | Asn Gln |
| | 530 | | | | | 535 | | | | 540 | | | | |
| Gln | Glu | Asp | Ile | Asn | Asn | Lys | Lys | Gln | Glu | Glu | Arg | Met | Leu | Lys |
| 545 | | | | | 550 | | | | 555 | | | | | 560 |
| Gln | Ile | Glu | Asn | Leu | Gln | Glu | Thr | Glu | Thr | Gln | Leu | Arg | Asn | Glu Leu |
| | | | 565 | | | | | 570 | | | | | | 575 |
| Glu | Tyr | Val | Arg | Glu | Glu | Leu | Lys | Gln | Lys | Arg | Asp | Glu | Val | Lys Cys |
| | | | 580 | | | | | 585 | | | | 590 | | |
| Lys | Leu | Asp | Lys | Ser | Glu | Glu | Asn | Cys | Asn | Asn | Leu | Arg | Lys | Gln Val |
| | 595 | | | | | | 600 | | | | | 605 | | |
| Glu | Asn | Lys | Asn | Lys | Tyr | Ile | Glu | Glu | Leu | Gln | Gln | Glu | Asn | Lys Ala |
| | 610 | | | | | 615 | | | | 620 | | | | |
| Leu | Lys | Lys | Lys | Gly | Thr | Ala | Glu | Ser | Lys | Gln | Leu | Asn | Val | Tyr Glu |
| 625 | | | | | 630 | | | | | 635 | | | | 640 |
| Ile | Lys | Val | Asn | Lys | Leu | Glu | Leu | Glu | Leu | Glu | Ser | Ala | Lys | Gln Lys |
| | | | 645 | | | | | 650 | | | | | | 655 |
| Phe | Gly | Glu | Ile | Thr | Asp | Thr | Tyr | Gln | Lys | Glu | Ile | Glu | Asp | Lys Lys |
| | | | 660 | | | | | 665 | | | | 670 | | |
| Ile | Ser | Glu | Asn | Leu | Leu | Glu | Glu | Val | Glu | Lys | Ala | Lys | Val | Ile |
| | 675 | | | | | 680 | | | | | 685 | | | |
| Ala | Asp | Glu | Ala | Val | Lys | Leu | Gln | Lys | Glu | Ile | Asp | Lys | Arg | Cys Gln |
| | 690 | | | | | 695 | | | | 700 | | | | |
| His | Lys | Ile | Ala | Glu | Met | Val | Ala | Leu | Met | Glu | Lys | His | Lys | His Gln |
| 705 | | | | | 710 | | | | | 715 | | | | 720 |
| Tyr | Asp | Lys | Ile | Ile | Glu | Glu | Arg | Asp | Ser | Glu | Leu | Gly | Leu | Tyr Lys |
| | | | 725 | | | | | 730 | | | | | | 735 |
| Ser | Lys | Glu | Gln | Glu | Gln | Ser | Ser | Leu | Arg | Ala | Ser | Leu | Glu | Ile Glu |
| | | | 740 | | | | | 745 | | | | | 750 | |
| Leu | Ser | Asn | Leu | Lys | Ala | Glu | Leu | Ser | Val | Lys | Lys | Gln | Leu | Glu |
| | 755 | | | | | | 760 | | | | | 765 | | |
| Ile | Glu | Arg | Glu | Glu | Lys | Glu | Lys | Leu | Lys | Arg | Glu | Ala | Lys | Glu Asn |
| | 770 | | | | | 775 | | | | | 780 | | | |
| Thr | Ala | Thr | Leu | Lys | Glu | Lys | Lys | Asp | Lys | Lys | Thr | Gln | Thr | Phe Leu |
| 785 | | | | | 790 | | | | | 795 | | | | 800 |
| Leu | Glu | Thr | Pro | Glu | Ile | Tyr | Trp | Lys | Leu | Asp | Ser | Lys | Ala | Val Pro |
| | | | 805 | | | | | 810 | | | | | | 815 |
| Ser | Gln | Thr | Val | Ser | Arg | Asn | Phe | Thr | Ser | Val | Asp | His | Gly | Ile Ser |
| | | | 820 | | | | | 825 | | | | | 830 | |
| Lys | Asp | Lys | Arg | Asp | Tyr | Leu | Trp | Thr | Ser | Ala | Lys | Asn | Thr | Leu Ser |
| | 835 | | | | | | 840 | | | | | 845 | | |
| Thr | Pro | Leu | Pro | Lys | Ala | Tyr | Thr | Val | Lys | Thr | Pro | Thr | Lys | Pro Lys |
| | 850 | | | | | 855 | | | | | 860 | | | |
| Leu | Gln | Gln | Arg | Glu | Asn | Leu | Asn | Ile | Pro | Ile | Glu | Glu | Ser | Lys Lys |
| 865 | | | | | 870 | | | | | 875 | | | | 880 |

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Lys | Arg | Lys | Met | Ala | Phe | Glu | Phe | Asp | Ile | Asn | Ser | Asp | Ser | Ser | Glu |
| | | | | 885 | | | | | 890 | | | | | 895 | |
| Thr | Thr | Asp | Leu | Leu | Ser | Met | Val | Ser | Glu | Glu | Glu | Thr | Leu | Lys | Thr |
| | | | 900 | | | | | 905 | | | | | 910 | | |
| Leu | Tyr | Arg | Asn | Asn | Asn | Pro | Pro | Ala | Ser | His | Leu | Cys | Val | Lys | Thr |
| | | 915 | | | | | | 920 | | | | 925 | | | |
| Pro | Lys | Lys | Ala | Pro | Ser | Ser | Leu | Thr | Thr | Pro | Gly | Pro | Thr | Leu | Lys |
| | 930 | | | | | 935 | | | | | 940 | | | | |
| Phe | Gly | Ala | Ile | Arg | Lys | Met | Arg | Glu | Asp | Arg | Trp | Ala | Val | Ile | Ala |
| 945 | | | | | 950 | | | | | 955 | | | | | 960 |
| Lys | Met | Asp | Arg | Lys | Lys | Lys | Leu | Lys | Glu | Ala | Glu | Lys | Leu | Phe | Val |
| | | | | 965 | | | | | 970 | | | | | 975 | |

<210> 93

<211> 3393

<212> DNA

<213> Homo sapiens

<400> 93

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<210> 94

<211> 188

<212> PRT

<213> Homo sapiens

<400> 94

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      20             25             30
Ser Lys Lys Glu Trp Glu Lys Met Lys Ser Ser Glu Lys Ile Val Tyr
      35             40             45
Val Tyr Met Lys Leu Asn Tyr Glu Val Met Thr Lys Leu Gly Phe Lys
      50             55             60
Val Thr Leu Pro Pro Phe Met Arg Ser Lys Arg Ala Ala Asp Phe His
      65             70             75             80
Gly Asn Asp Phe Gly Asn Asp Arg Asn His Arg Asn Gln Val Glu Arg
      85             90             95
Pro Gln Met Thr Phe Gly Ser Leu Gln Arg Ile Phe Pro Lys Ile Met
      100            105            110
Pro Lys Lys Pro Ala Glu Glu Glu Asn Gly Leu Lys Glu Val Pro Glu
      115            120            125
Ala Ser Gly Pro Gln Asn Asp Gly Lys Gln Leu Cys Pro Pro Gly Asn
      130            135            140
Pro Ser Thr Leu Glu Lys Ile Asn Lys Thr Ser Gly Pro Lys Arg Gly
      145            150            155            160
Lys His Ala Trp Thr His Arg Leu Arg Glu Arg Lys Gln Leu Val Val
      165            170            175
Tyr Glu Glu Ile Ser Asp Pro Glu Glu Asp Asp Glu
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<210> 95

<211> 576

<212> DNA

<213> Homo sapiens

<400> 95

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ctaggtttca aggtcaccct cccacctttc atgcgtagta aacgggctgc agacttcac 240
gggaatgatt ttggtaacga tcgaaaccac aggaatcagg ttgaacgtcc tcagatgact 300
ttcggcagcc tccagagaat cttcccgaag atcatgccca agaagccagc agaggaagaa 360

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cccccgggaa atccaagtac cttggagaag attaacaaga catctggacc caaaaggggg 480
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<210> 96
 <211> 94
 <212> PRT
 <213> Homo sapiens

<400> 96

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|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Pro | Ala | Thr | Gln | Arg | Gln | Asp | Pro | Ala | Ala | Ala | Gln | Glu | Gly | Glu | Asp |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | |
| Glu | Gly | Ala | Ser | Ala | Gly | Gln | Gly | Pro | Lys | Pro | Glu | Ala | Asp | Ser | Gln |
| | | | 20 | | | | | 25 | | | | | 30 | | |
| Glu | Gln | Gly | His | Pro | Gln | Thr | Gly | Cys | Glu | Cys | Glu | Asp | Gly | Pro | Asp |
| | | 35 | | | | | 40 | | | | | 45 | | | |
| Gly | Gln | Glu | Met | Asp | Pro | Pro | Asn | Pro | Glu | Glu | Val | Lys | Thr | Pro | Glu |
| | 50 | | | | | 55 | | | | | 60 | | | | |
| Glu | Glu | Met | Arg | Ser | His | Tyr | Val | Ala | Gln | Thr | Gly | Ile | Leu | Trp | Leu |
| 65 | | | | | 70 | | | | 75 | | | | | | 80 |
| Leu | Met | Asn | Asn | Cys | Phe | Leu | Asn | Leu | Ser | Pro | Arg | Lys | Pro | | |
| | | | | 85 | | | | | 90 | | | | | | |

<210> 97
 <211> 646
 <212> DNA
 <213> Homo sapiens

<400> 97

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<210> 98
 <211> 98
 <212> PRT
 <213> Homo sapiens

<400> 98

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|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| His | Cys | Pro | Thr | Glu | Asn | Glu | Pro | Asp | Leu | Ala | Gln | Cys | Phe | Phe | Cys |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | |
| Phe | Lys | Glu | Leu | Glu | Gly | Trp | Glu | Pro | Asp | Asp | Asp | Pro | Ile | Glu | Glu |
| | | | 20 | | | | | 25 | | | | | 30 | | |
| His | Lys | Lys | His | Ser | Ser | Gly | Cys | Ala | Phe | Leu | Ser | Val | Lys | Lys | Gln |
| | | 35 | | | | | 40 | | | | | 45 | | | |
| Phe | Glu | Glu | Leu | Thr | Leu | Gly | Glu | Phe | Leu | Lys | Leu | Asp | Arg | Glu | Arg |
| | 50 | | | | | 55 | | | | | 60 | | | | |
| Ala | Lys | Asn | Lys | Ile | Ala | Lys | Glu | Thr | Asn | Asn | Lys | Lys | Lys | Glu | Phe |
| 65 | | | | | 70 | | | | 75 | | | | | | 80 |
| Glu | Glu | Thr | Ala | Lys | Lys | Val | Arg | Arg | Ala | Ile | Glu | Gln | Leu | Ala | Ala |
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Met Asp

<210> 99
 <211> 1619
 <212> DNA
 <213> Homo sapiens

<400> 99
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<210> 100
 <211> 74
 <212> PRT
 <213> Homo sapiens

<400> 100
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 35 40 45
 Cys Glu Pro Val Val Pro Asn Ala Pro Pro Ala Tyr Glu Lys Leu Ser
 50 55 60
 Ala Glu Gln Ser Pro Pro Tyr Ser Pro
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<210> 101
 <211> 1524
 <212> DNA
 <213> Homo sapiens

<400> 101

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cggctgaaga ggccgctggg atcggcaccc tgacagtgat cctgggagtc ttactgctca 180
tcggctgttg gtattgtaga agacgaaatg gatacagagc cttgatggat aaaagtcttc 240
atgttggcac tcaatgtgcc ttaacaagaa gatgccaca agaagggttt gatcatcggg 300
acagcaaagt gtctcttcaa gagaaaaact gtgaacctgt ggttcccaat gctccacctg 360
cttatgagaa actctctgca gaacagtcac caccacctta ttcaccttaa gagccagcga 420
gacacctgag acatgctgaa attattttctc tcacactttt gcttgaattt aatacagaca 480
tctaattgtc tccttttgaa tgggtgtagga aaaatgcaag ccatctctaa taataagtca 540
gtgttaaaat tttagtaggt ccgctagcag tactaatcat gtgaggaaat gatgagaaat 600
attaaattgg gaaaactcca tcaataaatg ttgcaatgca tgatactato tgtgccagag 660
gtaatgttag taaatccatg gtgttatttt ctgagagaca gaattcaagt ggggtattctg 720
gggccatcca atttctcttt acttgaaatt tggctaataa caaactagtc aggttttcga 780
accttgaccg acatgaactg tacacagaat tgttccagta ctatggagtg ctacaaagg 840
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agcaatgtct ctttgtgctc taaaattcta ttatactaca ataatatatt gtaaagatcc 960
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ctcctgagta gctgggatta caggcgtgcc ccactatgcc tgactaattt tgtagtttta 1140
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ctgcccgcct cagcctccca aagtgtctga attacaggcg tgagccacca cgctggctg 1260
gatcctatat cttaggttaag acatataacg cagtctaatt acatttctact tcaaggctca 1320
atgctattct aactaatgac aagtattttc tactaaacca gaaattggta gaaggattta 1380
aataagtaaa agctactatg tactgcctta gtgctgatgc ctgtgtactg ccttaaatgt 1440
acctatggca atttagctct cttgggttcc caaatccctc tcacaagaat gtgcagaaga 1500
aatcataaag gatcagagat tctg 1524

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<210> 102

<211> 43

<212> PRT

<213> Homo sapiens

<400> 102

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Met Ala Ala Arg Ala Val Phe Leu Ala Leu Ser Ala Gln Leu Leu Gln
 1             5             10             15
Ala Arg Leu Met Lys Glu Glu Ser Pro Val Val Ser Trp Arg Leu Glu
      20             25             30
Pro Glu Asp Gly Thr Ala Leu Cys Phe Ile Phe
      35             40

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<210> 103

<211> 1004

<212> DNA

<213> Homo sapiens

<400> 103

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gtgggtggcaa cagagatggc agcgcagctg gagtgtagg agggcgccct gagcggtagg 180
agtggggctg gagcagtaag atggcgccca gagcggtttt tctggcattg tctgccagc 240
tgctccaagc caggctgatg aaggaggagt cccctgtggg gagctggagg ttggagcctg 300
aagacggcac agctctgtgc ttcactttct gaggttgtgg cagccacggg gatggagacg 360
gcagctcaac aggagcaata ggaggagatg gattttcact gtgtcagcca ggatggtctc 420
gatctcctga cctcgtgatc cgcccgccct ggccttccaa agtgccgaga ttacagcgat 480
gtgcattttg taagcacttt ggagccacta tcaaagtctg tgaagagaaa tgtacccaga 540
tgtatcatta tccttgtgct gcaggagccg gctcctttca ggatttctagt cacatcttcc 600
tgctttgtcc agaacacatt gaccaagctc ctgaaagatg taagtttact acgcatagac 660
ttttaaactt caaccaatgt atttactgaa aataacaaat gttgtaaatt ccctgagtgt 720
tattctactt gtattaaaag gtaataatac ataatacatta aaatctgagg gatcattgcc 780

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agagattgtt ggggagggaa atgttatcaa cggtttcatt gaaattaaat ccaaaaagtt 840
atttcctcag aaaaatcaaa taaagtttgc atgtttttta ttcttaaaac attttaaaaa 900
ccactgtaga atgatgtaaa tagggactgt gcagtatttc tgacatatat tataaaaatta 960
ttaaaaagtc aatcagtatt caacatcttt tacactaaaa agcc 1004

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<210> 104
<211> 9
<212> PRT
<213> Homo sapiens

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<400> 104
Trp Val Leu Thr Ala Ala His Cys Ile
1 5

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<210> 105
<211> 263
<212> PRT
<213> Homo sapiens

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<400> 105
Pro Met Trp Phe Leu Val Leu Cys Leu Ala Leu Ser Leu Gly Gly Thr
1 5 10 15
Gly Ala Ala Pro Pro Ile Gln Ser Arg Ile Val Gly Gly Trp Glu Cys
20 25 30
Glu Gln His Ser Gln Pro Trp Gln Ala Ala Leu Tyr His Phe Ser Thr
35 40 45
Phe Gln Cys Gly Gly Ile Leu Val His Arg Gln Trp Val Leu Thr Ala
50 55 60
Ala His Cys Ile Ser Asp Asn Tyr Gln Leu Trp Leu Gly Arg His Asn
65 70 75 80
Leu Phe Asp Asp Glu Asn Thr Ala Gln Phe Val His Val Ser Glu Ser
85 90 95
Phe Pro His Pro Gly Phe Asn Met Ser Leu Leu Glu Asn His Thr Arg
100 105 110
Gln Ala Asp Glu Asp Tyr Ser His Asp Leu Met Leu Leu Arg Leu Thr
115 120 125
Glu Pro Ala Asp Thr Ile Thr Asp Ala Val Lys Val Val Glu Leu Pro
130 135 140
Thr Gln Glu Pro Glu Val Gly Ser Thr Cys Leu Ala Ser Gly Trp Gly
145 150 155 160
Ser Ile Glu Pro Glu Asn Phe Ser Phe Pro Asp Asp Leu Gln Cys Val
165 170 175
Asp Leu Lys Ile Leu Pro Asn Asp Glu Cys Glu Lys Ala His Val Gln
180 185 190
Lys Val Thr Asp Phe Met Leu Cys Val Gly His Leu Glu Gly Gly Lys
195 200 205
Asp Thr Cys Val Gly Asp Ser Gly Gly Pro Leu Met Cys Asp Gly Val
210 215 220
Leu Gln Gly Val Thr Ser Trp Gly Tyr Val Pro Cys Gly Thr Pro Asn
225 230 235 240
Lys Pro Ser Val Ala Val Arg Val Leu Ser Tyr Val Lys Trp Ile Glu
245 250 255
Asp Thr Ile Ala Glu Asn Ser
260

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<210> 106
<211> 270
<212> PRT
<213> Homo sapiens

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<400> 106

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Pro Met Ile Arg Thr Leu Leu Leu Ser Thr Leu Val Ala Gly Ala Leu
 1          5          10          15
Ser Cys Gly Asp Pro Thr Tyr Pro Pro Tyr Val Thr Arg Val Val Gly
          20          25          30
Gly Glu Glu Ala Arg Pro Asn Ser Trp Pro Trp Gln Val Ser Leu Gln
          35          40          45
Tyr Ser Ser Asn Gly Lys Trp Tyr His Thr Cys Gly Gly Ser Leu Ile
          50          55          60
Ala Asn Ser Trp Val Leu Thr Ala Ala His Cys Ile Ser Ser Ser Arg
65          70          75          80
Thr Tyr Arg Val Gly Leu Gly Arg His Asn Leu Tyr Val Ala Glu Ser
          85          90          95
Gly Ser Leu Ala Val Ser Val Ser Lys Ile Val Val His Lys Asp Trp
          100          105          110
Asn Ser Asn Gln Ile Ser Lys Gly Asn Asp Ile Ala Leu Leu Lys Leu
          115          120          125
Ala Asn Pro Val Ser Leu Thr Asp Lys Ile Gln Leu Ala Cys Leu Pro
          130          135          140
Pro Ala Gly Thr Ile Leu Pro Asn Asn Tyr Pro Cys Tyr Val Thr Gly
145          150          155          160
Trp Gly Arg Leu Gln Thr Asn Gly Ala Val Pro Asp Val Leu Gln Gln
          165          170          175
Gly Arg Leu Leu Val Val Asp Tyr Ala Thr Cys Ser Ser Ser Ala Trp
          180          185          190
Trp Gly Ser Ser Val Lys Thr Ser Met Ile Cys Ala Gly Gly Asp Gly
          195          200          205
Val Ile Ser Ser Cys Asn Gly Asp Ser Gly Gly Pro Leu Asn Cys Gln
          210          215          220
Ala Ser Asp Gly Arg Trp Gln Val His Gly Ile Val Ser Phe Gly Ser
225          230          235          240
Arg Leu Gly Cys Asn Tyr Tyr His Lys Pro Ser Val Phe Thr Arg Val
          245          250          255
Ser Asn Tyr Ile Asp Trp Ile Asn Ser Val Ile Ala Asn Asn
          260          265          270

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<210> 107

<211> 270

<212> PRT

<213> Homo sapiens

<400> 107

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Pro Met Ile Arg Thr Leu Leu Leu Ser Thr Leu Val Ala Gly Ala Leu
 1          5          10          15
Ser Cys Gly Val Ser Thr Tyr Ala Pro Asp Met Ser Arg Met Leu Gly
          20          25          30
Gly Glu Glu Ala Arg Pro Asn Ser Trp Pro Trp Gln Val Ser Leu Gln
          35          40          45
Tyr Ser Ser Asn Gly Gln Trp Tyr His Thr Cys Gly Gly Ser Leu Ile
          50          55          60
Ala Asn Ser Trp Val Leu Thr Ala Ala His Cys Ile Ser Ser Ser Arg
65          70          75          80
Ile Tyr Arg Val Met Leu Gly Gln His Asn Leu Tyr Val Ala Glu Ser
          85          90          95
Gly Ser Leu Ala Val Ser Val Ser Lys Ile Val Val His Lys Asp Trp
          100          105          110
Asn Ser Asn Gln Val Ser Lys Gly Asn Asp Ile Ala Leu Leu Lys Leu
          115          120          125
Ala Asn Pro Val Ser Leu Thr Asp Lys Ile Gln Leu Ala Cys Leu Pro

```

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| 130 | | 135 | | 140 | | | | | | | | | | | |
| Pro | Ala | Gly | Thr | Ile | Leu | Pro | Asn | Asn | Tyr | Pro | Cys | Tyr | Val | Thr | Gly |
| 145 | | | | | 150 | | | | | 155 | | | | | 160 |
| Trp | Gly | Arg | Leu | Gln | Thr | Asn | Gly | Ala | Leu | Pro | Asp | Asp | Leu | Lys | Gln |
| | | | | 165 | | | | | | 170 | | | | | 175 |
| Gly | Arg | Leu | Leu | Val | Val | Asp | Tyr | Ala | Thr | Cys | Ser | Ser | Ser | Gly | Trp |
| | | | | 180 | | | | | | 185 | | | | | 190 |
| Trp | Gly | Ser | Thr | Val | Lys | Thr | Asn | Met | Ile | Cys | Ala | Gly | Gly | Asp | Gly |
| | | 195 | | | | | 200 | | | | | | 205 | | |
| Val | Ile | Cys | Thr | Cys | Asn | Gly | Asp | Ser | Gly | Gly | Pro | Leu | Asn | Cys | Gln |
| | 210 | | | | | | 215 | | | | | 220 | | | |
| Ala | Ser | Asp | Gly | Arg | Trp | Glu | Val | His | Gly | Ile | Gly | Ser | Leu | Thr | Ser |
| 225 | | | | | 230 | | | | | 235 | | | | | 240 |
| Val | Leu | Gly | Cys | Asn | Tyr | Tyr | Tyr | Lys | Pro | Ser | Ile | Phe | Thr | Arg | Val |
| | | | | 245 | | | | | 250 | | | | | | 255 |
| Ser | Asn | Tyr | Asn | Asp | Trp | Ile | Asn | Ser | Val | Ile | Ala | Asn | Asn | | |
| | | | 260 | | | | | 265 | | | | | 270 | | |

<210> 108
 <211> 9
 <212> PRT
 <213> Homo sapiens

<400> 108
 Asn Ile Tyr Asp Leu Phe Val Trp Met
 1 5

<210> 109
 <211> 10
 <212> PRT
 <213> Homo sapiens

<400> 109
 Tyr Asp Leu Phe Val Trp Met His Tyr Tyr
 1 5 10

<210> 110
 <211> 9
 <212> PRT
 <213> Homo sapiens

<400> 110
 Asp Leu Phe Val Trp Met His Tyr Tyr
 1 5

<210> 111
 <211> 9
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<400> 111
 Asp Ala Leu Leu Gly Gly Ser Glu Ile
 1 5

<210> 112
 <211> 10

<212> PRT
<213> Homo sapiens

<400> 112
Gly Ser Glu Ile Trp Arg Asp Ile Asp Phe
1 5 10

<210> 113
<211> 9
<212> PRT
<213> Homo sapiens

<400> 113
Ser Glu Ile Trp Arg Asp Ile Asp Phe
1 5

<210> 114
<211> 9
<212> PRT
<213> Homo sapiens

<400> 114
Glu Ile Trp Arg Asp Ile Asp Phe Ala
1 5

<210> 115
<211> 10
<212> PRT
<213> Homo sapiens

<400> 115
Leu Gln Glu Val Tyr Pro Glu Ala Asn Ala
1 5 10

<210> 116
<211> 10
<212> PRT
<213> Homosapiens

<400> 116
Glu Val Tyr Pro Glu Ala Asn Ala Pro Ile
1 5 10

<210> 117
<211> 9
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<213> Homosapiens

<400> 117
Val Tyr Pro Glu Ala Asn Ala Pro Ile
1 5

<210> 118
<211> 8
<212> PRT

<213> Homosapiens

<400> 118

Tyr Pro Glu Ala Asn Ala Pro Ile
1 5

<210> 119

<211> 10

<212> PRT

<213> Homosapiens

<400> 119

Tyr Pro Glu Ala Asn Ala Pro Ile Gly His
1 5 10

<210> 120

<211> 10

<212> PRT

<213> Homosapiens

<400> 120

Ala Pro Ile Gly His Asn Arg Glu Ser Tyr
1 5 10

<210> 121

<211> 9

<212> PRT

<213> Homosapiens

<400> 121

Pro Ile Gly His Asn Arg Glu Ser Tyr
1 5

<210> 122

<211> 10

<212> PRT

<213> Homosapiens

<400> 122

Pro Ile Gly His Asn Arg Glu Ser Tyr Met
1 5 10

<210> 123

<211> 10

<212> PRT

<213> Homosapiens

<400> 123

Ala Pro Ile Gly His Asn Arg Glu Ser Tyr
1 5 10

<210> 124

<211> 9

<212> PRT

<213> Homosapiens

<400> 124

Pro Ile Gly His Asn Arg Glu Ser Tyr
1 5

<210> 125

<211> 8

<212> PRT

<213> Homosapiens

<400> 125

Glu Ser Tyr Met Val Pro Phe Ile
1 5

<210> 126

<211> 10

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<213> Homosapiens

<400> 126

Glu Ser Tyr Met Val Pro Phe Ile Pro Leu
1 5 10

<210> 127

<211> 9

<212> PRT

<213> Homosapiens

<400> 127

Ser Tyr Met Val Pro Phe Ile Pro Leu
1 5

<210> 128

<211> 10

<212> PRT

<213> Homosapiens

<400> 128

Ser Tyr Met Val Pro Phe Ile Pro Leu Tyr
1 5 10

<210> 129

<211> 9

<212> PRT

<213> Homosapiens

<400> 129

Tyr Met Val Pro Phe Ile Pro Leu Tyr
1 5

<210> 130

<211> 9

<212> PRT

<213> Homosapiens

<400> 130

Met Val Pro Phe Ile Pro Leu Tyr Arg
1 5

<210> 131

<211> 10

<212> PRT

<213> Homosapiens

<400> 131

Met Val Pro Phe Ile Pro Leu Tyr Arg Asn
1 5 10

<210> 132

<211> 8

<212> PRT

<213> Homosapiens

<400> 132

Val Pro Phe Ile Pro Leu Tyr Arg
1 5

<210> 133

<211> 8

<212> PRT

<213> Homosapiens

<400> 133

Ile Pro Leu Tyr Arg Asn Gly Asp
1 5

<210> 134

<211> 10

<212> PRT

<213> Homosapiens

<400> 134

Ile Pro Leu Tyr Arg Asn Gly Asp Phe Phe
1 5 10

<210> 135

<211> 9

<212> PRT

<213> Homosapiens

<400> 135

Pro Leu Tyr Arg Asn Gly Asp Phe Phe
1 5

<210> 136

<211> 10

<212> PRT

<213> Homosapiens

<400> 136

Pro Leu Tyr Arg Asn Gly Asp Phe Phe Ile
1 5 10

<210> 137
<211> 10
<212> PRT
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<400> 137
Arg Asn Gly Asp Phe Phe Ile Ser Ser Lys
1 5 10

<210> 138
<211> 9
<212> PRT
<213> Homosapiens

<400> 138
Asn Gly Asp Phe Phe Ile Ser Ser Lys
1 5

<210> 139
<211> 9
<212> PRT
<213> Homosapiens

<400> 139
Tyr Ile Lys Ser Tyr Leu Glu Gln Ala
1 5

<210> 140
<211> 9
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<213> Homosapiens

<400> 140
Ser Tyr Leu Glu Gln Ala Ser Arg Ile
1 5

<210> 141
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<213> Homosapiens

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Glu Gln Ala Ser Arg Ile Trp Ser Trp Leu
1 5 10

<210> 142
<211> 9
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<213> Homosapiens

<400> 142
Gln Ala Ser Arg Ile Trp Ser Trp Leu

1 5

<210> 143
<211> 8
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<213> Homosapiens

<400> 143
Ala Ser Arg Ile Trp Ser Trp Leu
1 5

<210> 144
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<212> PRT
<213> Homosapiens

<400> 144
Ala Ser Arg Ile Trp Ser Trp Leu Leu
1 5

<210> 145
<211> 9
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<400> 145
Arg Ile Trp Ser Trp Leu Leu Gly Ala
1 5

<210> 146
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<400> 146
Gly Pro Ala Tyr Ser Gly Arg Glu Ile
1 5

<210> 147
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<213> Homosapiens

<400> 147
Gly Pro Ala Tyr Ser Gly Arg Glu Ile Ile
1 5 10

<210> 148
<211> 8
<212> PRT
<213> Homosapiens

<400> 148
Pro Ala Tyr Ser Gly Arg Glu Ile
1 5

<210> 149
<211> 9
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<400> 149
Pro Ala Tyr Ser Gly Arg Glu Ile Ile
1 5

<210> 150
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<400> 150
Pro Ala Tyr Ser Gly Arg Glu Ile Ile Tyr
1 5 10

<210> 151
<211> 9
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<400> 151
Ala Tyr Ser Gly Arg Glu Ile Ile Tyr
1 5

<210> 152
<211> 9
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<400> 152
Gly Arg Glu Ile Ile Tyr Pro Asn Ala
1 5

<210> 153
<211> 10
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<400> 153
Arg Glu Ile Ile Tyr Pro Asn Ala Ser Leu
1 5 10

<210> 154
<211> 9
<212> PRT
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<400> 154
Glu Ile Ile Tyr Pro Asn Ala Ser Leu
1 5

<210> 155
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Glu Ile Ile Tyr Pro Asn Ala Ser Leu Leu
1 5 10

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<211> 8
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<400> 156
Ile Ile Tyr Pro Asn Ala Ser Leu
1 5

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<400> 157
Ile Ile Tyr Pro Asn Ala Ser Leu Leu
1 5

<210> 158
<211> 10
<212> PRT
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<400> 158
Ile Ile Tyr Pro Asn Ala Ser Leu Leu Ile
1 5 10

<210> 159
<211> 8
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<400> 159
Tyr Pro Asn Ala Ser Leu Leu Ile
1 5

<210> 160
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<400> 160
Leu Leu Ile Gln Asn Ile Ile Gln Asn Asp
1 5 10

<210> 161
<211> 10
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Glu Glu Ala Thr Gly Gln Phe Arg Val Tyr
1 5 10

<210> 162
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<400> 162
Glu Ala Thr Gly Gln Phe Arg Val Tyr
1 5

<210> 163
<211> 9
<212> PRT
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<400> 163
Tyr Pro Glu Leu Pro Lys Pro Ser Ile
1 5

<210> 164
<211> 8
<212> PRT
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<400> 164
Pro Glu Leu Pro Lys Pro Ser Ile
1 5

<210> 165
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<400> 165
Arg Ser Asp Ser Val Ile Leu Asn Val
1 5

<210> 166
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<400> 166
Arg Ser Asp Ser Val Ile Leu Asn Val Leu
1 5 10

<210> 167

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<400> 167
Ser Asp Ser Val Ile Leu Asn Val Leu
1 5

<210> 168
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<400> 168
Ser Asp Ser Val Ile Leu Asn Val Leu Tyr
1 5 10

<210> 169
<211> 9
<212> PRT
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<400> 169
Asp Ser Val Ile Leu Asn Val Leu Tyr
1 5

<210> 170
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<400> 170
Val Leu Tyr Gly Pro Asp Ala Pro Thr Ile
1 5 10

<210> 171
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Leu Tyr Gly Pro Asp Ala Pro Thr Ile
1 5

<210> 172
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<400> 172
Tyr Gly Pro Asp Ala Pro Thr Ile
1 5

<210> 173
<211> 10

<212> PRT
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<400> 173
Gly Pro Asp Ala Pro Thr Ile Ser Pro Leu
1 5 10

<210> 174
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<212> PRT
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<400> 174
Pro Asp Ala Pro Thr Ile Ser Pro Leu
1 5

<210> 175
<211> 8
<212> PRT
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<400> 175
Asp Ala Pro Thr Ile Ser Pro Leu
1 5

<210> 176
<211> 9
<212> PRT
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<400> 176
Ala Pro Thr Ile Ser Pro Leu Asn Thr
1 5

<210> 177
<211> 10
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<400> 177
Pro Thr Ile Ser Pro Leu Asn Thr Ser Tyr
1 5 10

<210> 178
<211> 9
<212> PRT
<213> Homosapiens

<400> 178
Thr Ile Ser Pro Leu Asn Thr Ser Tyr
1 5

<210> 179
<211> 10
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<213> Homosapiens

<400> 179

Pro Thr Ile Ser Pro Leu Asn Thr Ser Tyr
1 5 10

<210> 180

<211> 9

<212> PRT

<213> Homosapiens

<400> 180

Thr Ile Ser Pro Leu Asn Thr Ser Tyr
1 5

<210> 181

<211> 10

<212> PRT

<213> Homosapiens

<400> 181

Asn Thr Ser Tyr Arg Ser Gly Glu Asn Leu
1 5 10

<210> 182

<211> 9

<212> PRT

<213> Homosapiens

<400> 182

Thr Ser Tyr Arg Ser Gly Glu Asn Leu
1 5

<210> 183

<211> 8

<212> PRT

<213> Homosapiens

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Ser Tyr Arg Ser Gly Glu Asn Leu
1 5

<210> 184

<211> 10

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<213> Homosapiens

<400> 184

Ser Tyr Arg Ser Gly Glu Asn Leu Asn Leu
1 5 10

<210> 185

<211> 9

<212> PRT

<213> Homosapiens

<400> 185

Tyr Arg Ser Gly Glu Asn Leu Asn Leu
1 5

<210> 186

<211> 9

<212> PRT

<213> Homosapiens

<400> 186

Ser Gly Glu Asn Leu Asn Leu Ser Cys
1 5

<210> 187

<211> 10

<212> PRT

<213> Homosapiens

<400> 187

Glu Asn Leu Asn Leu Ser Cys His Ala Ala
1 5 10

<210> 188

<211> 9

<212> PRT

<213> Homosapiens

<400> 188

Asn Leu Asn Leu Ser Cys His Ala Ala
1 5

<210> 189

<211> 10

<212> PRT

<213> Homosapiens

<400> 189

His Ala Ala Ser Asn Pro Pro Ala Gln Tyr
1 5 10

<210> 190

<211> 9

<212> PRT

<213> Homosapiens

<400> 190

Ala Ala Ser Asn Pro Pro Ala Gln Tyr
1 5

<210> 191

<211> 10

<212> PRT

<213> Homosapiens

<400> 191
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|-----|-----|-----|-----|-----|-----|-----|-----|-----|
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|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
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